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ON

BERI-BERI

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CONTENTS

1. ACTON, H.W. Problem of epidemic dropsy and beriberi. . . . 1925

2. BRADDON, W.L. Discovery of the cause of beri-beri. . . . 1911

3. CORLETTE, C.E. General account of beriberi as seen in Sydney. 1895

4. DURHAM, H.E. Some notes on the urine in beri-beri. . . . 1904

5. ELDRIDGE, S. On beri-beri. 1880

6. GRATEROL Y MORLES, J. Contribucion al estudio del beriberi. 1930

7. JOLLY, G.G. Beriberi in Cheduba Island, Arakan, Burma. . . . 1930

8. MARSHALL, D.G. Beri-beri: an infected European crew at Leith. 1906

9. NORMAN, C. On beri-beri occurring in temperate climates. 1898

10. - - - - - Clinical features of beri-beri. 1899

11. ROST, E.R. The cause of beri-beri. 1900

12. SHIMER, I.A. Beriberi on the Isthmus of Panama. . . . 1907

13. SINCLAIR, A.W. Notes on beri-beri. 1889

14. VALENZUELA, A.J. Beriberi. 1922

15. VERSCHUUR, A.F. & IJSSELSTEYN, G. van. Epidemic disease in the Richmond District Asylum. . . . 1900

BERIBERI (5
P.4348

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THE PROBLEM OF EPIDEMIC DROPSY AND BERIBERI.*

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Introduction.—Up to the present time, the general consensus of opinion has been that the two closely allied diseases, beriberi and epidemic dropsy are caused by some deficiency of an essential substance (vitamine) in the diet. We look upon these two diseases as belonging to a group syndrome, where the three main signs are œdema, hypertrophy followed by dilatation of the heart, and peripheral neuritis. In epidemic dropsy usually only two of these signs are present, i.e., the œdema and the effects on the heart, and in dry beriberi there are cardiac lesions, marked peripheral neuritis but little or no œdema. Between these extremes, there are overlapping cases where these three signs vary in extent. We can therefore compare it to a syndrome like asthma where there are diverse poisons all producing the characteristic signs of this condition, viz., bronchial spasm and turgescence of the mucous membrane, but in varying extent; so that we get cases of almost pure bronchial spasm and others largely with bronchial turgescence. As will be seen later, we consider the cause of this syndrome of beriberi to be due to certain poisons elaborated in the food which is improperly stored; thus we have seen these symptoms and signs produced by rice, by the exclusive use of tinned provisions (Mesopotamia and Calcutta), and in Labrador it is stated that eating dried codfish causes this disease. The upholders of the rice theory immediately advance the argument; did these people eat rice, say as puddings, or was the flour adulterated by the cheaper rice flour ? There is no need for this refinement, as we know that provided the same proteins or amino-acids are present, the decomposition of an amino-acid-like tryptophane to indol is not the exclusive property of a single proteid or single species of bacteria. We can safely say however that the vast majority of cases seen in clinical practice occur amongst those whose main article of diet is rice.

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The first point that has to be settled is whether the disease is due to eating rice or not ? The following objections have been raised against the rice theory in Castellam's "Text-Book on Tropical Medicine," (1919), page 1677.

(*i*) "Beriberi may occur in people who do not feed on rice. We have seen an epidemic amongst officers on a man-of-war." Against this objection we may state that beriberi occurs—though rarely—amongst British troops who are not rice eaters, but who take a certain amount of rice as rice puddings or in lieu of potatoes, as in Mesopotamia during the war. The rice issued is frequently diseased, e.g., on the *R. I. M. S. Investigator* in the Persian Gulf. Moreover under these conditions there is a large amount of tinned provisions used as food.

(*ii*) *The geographical distribution.*—" In populations eating the same kind of rice, some suffer from beriberi and others do not." In Bengal, epidemic dropsy is a disease of the middle class Hindoos, whose diet is mainly rice. The neighbouring Mohamedan population, although eating the same rice, take a smaller quantity of it owing to the inclusion of bread, meat, etc., in their diet. Again, the poorest classes live largely on a small grained rice of a coarse quality, but freshly milled, and rarely suffer from this disease.

(*iii*) " Tamil coolies in Ceylon do not get beriberi though they suffer from this disease in the Straits Settlements. In both countries they are mostly supplied by the same kind of rice, Rangoon rice." Our experiments show that a hot moist climate is necessary, such as occurs in Calcutta during the middle of July to September for infection to take place in the rice, thus explaining the peculiar distribution of the disease.

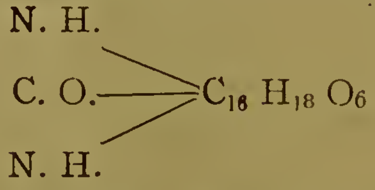
(*iv*) " People recovered from beriberi go back to their usual rice diet without suffering from the disease. Thus in the Malay States the mortality is only 20 per cent. therefore 80 per cent. of the sufferers recover. Do these people change their diet?" Our contention is that the disease is due to infection of the grain and the formation of poisonous bases. As long as healthy grain is eaten no disease occurs. Conversely as soon as the supply of diseased grain is exhausted, they then live on healthy grain and without any change in the diet recover, irrespective of avitaminosis.

Now having considered that we have satisfactorily answered these objections raised by Castellani against the rice theory, and moreover that all the ætiological factors point to the same conclusion, we can safely assert that in the vast majority of cases, both beriberi and epidemic dropsy are diseases produced by eating rice.

Eijkman, in 1897, showed that prisoners fed on red unpolished rice escaped the disease, whilst those fed on white polished rice were very apt to suffer from beriberi. Both he and Voderman considered that this was due to a loss in the protection of the grain. Fraser however failed to produce beriberi in prisoners fed on polished rice. The difference between these two forms of grain is that white rice is deprived of the peripheral layer during the milling processes.

The works of Eijkman, Braddon, Vedder and Chamberlain have made it sufficiently clear that beriberi is caused by eating *polished rice* and is prevented by eating unpolished rice.

Casimir Funk described a base that was present in the pericarpal layers, a diamine belonging to the pyramidine group and of the following constitutional formula:—



$$\left.\begin{matrix}\mathrm{N.\,H.}\\ \mathrm{C.\,O.}\!-\!\!-\!\!-\\ \mathrm{N.\,H.}\end{matrix}\right> \mathrm{C_{16}\,H_{18}\,O_6}$$

This base is soluble in water, alcohol, dialyzable and can stand heat up to 130°C.: it is present in the proportion of 0.1 gramme per kilogramme of rice polishings:—the term polishing is often held to include rice bran and the polishings. Funk regards this base as an essential to the nervous tissue metabolism, and if not present in sufficient quantities, the nerves break down and as a result beriberi occurs in the individual. In 1917, Chick and Hume showed that in order to keep a person in health there must be (1) a proper supply of proteins, carbohydrates, fats, salts, and water, (2) an adequate amount of vitamines. These vitamines have not been isolated in a pure state in order to determine their chemical composition, but some are water-soluble, others alcohol—and others fat-soluble. They can stand a temperature up to 100°C., but are destroyed at 120°C. The vitamine of importance in beriberi has been named the anti-neuritic or anti-beriberi vitamine, the first includes the polyneuritis of fowls. The vitamine theory in some form is universally accepted at the present time to explain the cause of these so-called deficiency diseases.

Manson brought forward the hypothesis that a germ may be present in the soil, house, or ship, and under certain conditions of temperature and moisture may grow and produce toxins which when ingested cause the disease. Moreover, this germ may be carried by man from place to place. He also pointed out that the disease clings to ships, and appears year after year when the tropics are reached. In support of this theory he points out (1) that when patients are removed from an epidemic area they at once begin to recover; (2) he quotes Hirota's observations, that 52 infants nursed by beriberi mothers showed signs of the disease and did not improve when treated medicinally, but when taken from these mothers and placed with a wet-nurse or on artificial foods rapidly improved. He rightly points out that these children must have been poisoned by some chemical substance and not infected with a germ. But of course the germ producing the toxin might be in the mother's body.

Yamagriva considers beriberi to be caused when the rice is improperly stored or preserved as it occurs even when this rice is well boiled. Braddon ascribes the disease to the ingestion of a poison found in the rice which is the result of a specific product of some organism, epiphyte or parasite, but he does not believe the disease to be due to the ingestion of the organism.

This briefly is the present position of the beriberi problem.

(*a*) The majority of observers consider that it is a deficiency disease due to the lack of an essential vitamine.

(*b*) A few consider that it is due to a poison produced in the grain by some organism or by defective preservation or storage.

Our work commenced with the production of certain poisonous bases produced in an amino-acid broth by the *B. dysentericæ* (Shiga) 1922. Again in the same year when working on lathyrism which is caused by eating *kesari dal* (*Lathyrus sativus*), we found certain bases, not alkaloids, by which we were able to produce the disease in animals. On going away on furlough, Colonel Megaw handed us over the results of his clinical and statistical enquiry into the causation of this disease, which he has now published (1923). Naturally as we had been working at these bases, the first thought that occurred to us was whether we were dealing with a similar problem to ergotism, where alkaloids and bases can be produced by the *Claviceps purpurea* from the proteids of rye; these are able to cause vaso-constriction (gangrene) and neuritis sensory (anæsthesia). In beriberi, which is due to rice eating, the symptoms caused are due to an increased capillary permeability (œdema) and a neuritis motor (paralysis). The problem that lay before us was to identify the diseased rice from the healthy, to isolate the organism producing the disease in the rice grains, and to separate the bases, and reproduce experimentally in animals the symptoms produced in man. On the other hand we could not totally disregard the vitamine theory, when such skilled workers as Hayden, DeSilva, Chick, Hume, Moore and Webster had made this theory acceptable to the medical profession. We hoped by our experimental data to harmonise these two opposite views on beriberi, and to show that when the pericarp is removed by polishing, there is lost, not only the mechanical protection of the grain, but also valuable antagonistic substances. Under certain conditions of temperature and humidity, especially if rice is stored in infected godowns the rice rapidly becomes diseased. This diseased rice contains bases that cause a rise of limb volume with a fall of blood pressure, indicating œdema, increase in the amplitude of the heart-beat explaining the hypertrophy, and a rise in intra-ocular tension, the cause of glaucoma in epidemic dropsy.

If we consider beriberi to be produced in a similar way to asthma we will have three things to consider:—

(1) The nature of the poisons produced.

(2) The endocrine mechanism.

(3) The state of the nerve endings that receive these poisons.

During the last three years we have had several difficulties to contend with before we were able to complete this work. In the first place when we commenced working on rices, that caused epidemic dropsy we were able to show the existence of substances that produced a rise in the limb volume and an increase in the intra-ocular tension, but when working on Burma rice we were hardly able to demonstrate the presence of these bases, and it was a long time before we realized the difference in the chemical composition of these two rices. Again, we found that animals varied widely in their reactions towards these poisons: this meant the investigation of the causes of susceptibility, and our results were published in *The Indian Medical Gazette* for July 1924.

The neurotoxic principle again proved a stumbling block until we discovered it was alcohol-soluble and not water-soluble and moreover that it paralysed the para-sympathetic. The last difficulty to be overcome was the production of these bases in sterile media from laboratory cultures. For a long time, when growing the cultures ærobically, we were only able to produce the water-soluble bases. It was not until we realized the anærobic thermophilic nature of rice decomposition, that we were able to produce the neurotoxin by raising the incubator temperature to 50°C. and making the cultures anærobic.

THE INFLUENCE OF THE SUBSTRATE.

Before we can appreciate the differences in the different grades of rice, we must be able to judge the character of the fruit. The usual classification adopted by the market has been to name a rice after some prominent character, e.g., *Patni,* from the centre of export; *Peshawari,* because it was handled by up-country merchants; *Basmati,* fine flavoured, etc. A better idea of the quality of the rice can be obtained by the following description which we have evolved in trying to understand, how rice caused epidemic dropsy or beriberi.

The texture of the fruit. By the water test, two main varieties are seen by looking at the grain in water—

(*a*) Coarsed grained fruit: the grains may be short and plump such as the Burmah rice, or long and plump like the *desi* or indigenous rice, e.g., *Ashu, Nagra, Patni.* The grain has a horny-like appearance, and is known to be not very digestible, but sweeter. These rices are new, sell at from 5½ to 6 seers to the rupee, and are eaten by the poorer classes. When allowed to season, they give a very sweet rice which is mainly used for *payesh* (rice cooked in milk).

(*b*) Finer grade rice: the fruit may be long and fine like the *dadkhani,* or long and medium such as the *Peshawari* and *Kaminibhog,* etc. The grain is semi-translucent and the better the grade the more waxy is the appearance. These rices are more digestible and command a higher price, from 3½ to 1 seer for the rupee, and are usually eaten by the middle and upper classes. When allowed to season, this class produces a very digestible rice, which is eaten with curry, *dal,* etc.

The quality is also dependant on the crop. Thus in Bengal there are two main crops in the year—

(*i*) The *aus* or early crop is sown broadcast in April, and is reaped during July and August and September. It is generally regarded as being poorer in quality, very indigestible and causing diarrhœa. It is eaten by the poor, and is also used as food for animals.

(*ii*) The *aman* or winter crop is the better crop of the year: the rice is transplanted in June, July and August and is harvested in November and December, it is spoken of as the *chotan aman.* This is the rice that is largely eaten by the middle class Bengali families. The *boran aman* is a coarser kind of rice sown broadcast in the beds of the *jheels,* and in very low-lying land in May, and gathered in December and January.

The *boro* or spring rice is far less important than the above mentioned crops and rarely comes into the markets of larger towns. We have therefore two grades of rice—

(*a*) The coarser rice: more horny in appearance, more indigestible and eaten by the poorer classes owing to its cheapness. It is largely derived from the *aus, boran aman* and *boro* crops—and as we will see later this rice is concerned with beriberi.

(*b*) The medium and finer grades: more waxy in appearance and more digestible and eaten by the middle and better classes. This is derived mainly from the *chotan aman* crop, and if diseased causes epidemic dropsy.

In Bengal, epidemic dropsy is a disease of the middle class Bengali, whose main article of diet is the medium grades of rice; whereas the Chinaman, who lives on the highly polished coarser rice, suffers from beriberi. The distinction between the two diseases is very fine; in epidemic dropsy, œdema and the effect on the heart are prominent, whilst glaucoma and a slight degree of neuritis is sometimes seen. In beriberi, the neuritis and the heart signs are always marked, but the œdema may or may not be present and glaucoma is rare. The poisons produced in the two substrates cannot be identical in amount, but in extreme cases, i.e., dry beriberi and epidemic dropsy without loss of knee-jerks, the poisons can be readily separated in the rices, but there must necessarily be a good deal of overlapping when the substrates are like each other in chemical composition, e.g., when the medium grades approach the coarser quality.

THE PREPARATION OF THE RICE FOR THE MARKET.

(*a*) The husks are prepared for removal from the *paddy* or *dhan* in one of the three ways—(*i*) *Atap* or sun-dried rice, is prepared by soaking the paddy in cold water for 24 hours, and then the grains are dried in the sun by being spread out in thin layers on cemented or specially prepared platforms, hence the name *atap* or sun-dried. This rice is generally eaten by orthodox Brahmins, widows, and at certain festivals, for the Brahmins are not allowed to eat food other than that cooked by their own hands. This method of preparation of the rice does not destroy the enzymes of the grain. (*ii*) *Balam* rice consists of *paddy* which is husked after hot water has been sprinkled on it. The water inflates the grain, and when dry facilitates the removal of the husk. The heat is not sufficient to kill the enzymes or coagulate the proteids, but avoids the number of hours that are required to swell the grain by simple steeping in cold water. (*iii*) *Siddha* or parboiled rice is prepared by soaking the *paddy* in large vessels and then the water is brought up to the boil. The parboiling kills most of the enzymes, and coagulates the surface proteids in the grain. This parboiled rice is dried on platforms before it is husked. Rice from over-steeped *paddy* is dark in colour, and when overboiled is coarse in appearance, and in the milling it is often broken up into fragments. It will be seen that the better and medium grades of rice used for ceremonial purposes (*atap*) or otherwise (*balam*) are generally steeped in cold water or hot water respectively in order to preserve the enzymes of the grain and allow the seasoning processes to follow when the grain is properly stored. The medium and coarser grades are more often parboiled as it is easier to separate the husks.

(*b*) The removal of the husks may be carried out in two ways—(*i*) *Anchatta,* by hand: this is generally done in the villages with a wooden pestle and mortar, or by it being beaten on a platform with a wooden beam (*dhenki*). The *paddy* is stored as such, and, when required, a small amount is taken out, say a 2 to 4 weeks' supply. The husks are prepared for removal, and the hand pounding leaves a good deal of the pericarp on the grain. During this process many of the grains are broken, and *atap* with entire grains sells at a higher price than the *siddha* or parboiled rice, although made from the same *paddy*. (*ii*) *Kalchatta* or machine removal is carried out where mills are available in the large towns. In the first place the hulls are removed by passing the grain through milling stones, screens, and winnowing machines. The kernels are then decorticated, and the outer cuticle with much of the gluten layer of the grain and the embryo are removed: this constitutes the rice bran or meal. This rice is known as unpolished rice.

(*c*) The polishing process is the final process which the grain undergoes. The polished grain is placed in rotating cylinders of wood and wire gauze, the surface of which is covered with soft tanned hide. In this process a film of gluten and starch cells is removed, and the fine powder thus obtained is technically called rice polishings: the polished grains are then screened in various grades and sizes.

These terms such as *atap, balam,* etc., are not the names of different rices but of various processes which the grain goes through before it arrives on the market.

We are now in a position to appreciate the fact that parboiled polished rice is the most dangerous type of process to subject rice to, because all the living cells and enzymes of the grain have been killed by the heat, and the machine-milling and polishing has removed the embryo and the delicate starch cells, so that raw surfaces are exposed to the attack of bacteria and fungi. This rice, as we shall show later, when stored under favourable conditions of temperature and humidity is likely to become diseased, and so produce epidemic dropsy or beriberi. In villages the removal of the husk is facilitated by sun-drying or steeping, the husk is removed by hand, which leaves much of the pericarp and the whole of the gluten layer, only small quantities are prepared at a time so that a sufficient time is not allowed to elapse for gross invasion of the grain.

These factors all combine to explain the comparative immunity of the villagers to epidemic dropsy.

The seasoning of the rice.—Everyday experience has shown that new rice is indigestible, but if kept for some time—six months or more—the rice becomes more digestible and sweeter. Thus the rices can still further be subdivided into—

(*a*) New rice which is more indigestible, cheaper, and is the type usually eaten by the poorer classes and villagers. As a rule no preservatives are added and it is eaten soon after being turned out from the mills. Hence these diseases are not seen amongst persons eating this rice, as there is usually not sufficient time for it to get diseased. With imperfect storage in godowns or in transportation, this parboiled highly polished rice rapidly becomes diseased as no preservatives are added, and then beriberi is seen amongst those who consume the rice under these conditions.

(*b*) *Seasoned rice.*—The better classes demand a rice for one of its two qualities, (*i*) digestibility, (*ii*) sweetness. The seasoning of rice takes some months in storage to effect the hydrolysis of the insoluble proteids and carbohydrates into the more soluble proteoses, peptones and sugars. These characters are brought about mainly as the result of the hydrolysis of the proteids and carbohydrates by enzyme action. Such rices are either sun-dried or steeped and never parboiled, although they may be highly polished. Thus the Marwaris eat this rice mainly as *kher* (i.e., rice boiled in milk and eaten as a porridge) and so require the rice digestible and sweet, whilst the Bengalis and Mohamedans who eat their rice with *tarkari* or curry do not require it to be sweet, as the latter flavour would interfere with the high seasonings of the curry. Such rices are carefully selected and preserved from bacterial or fungal attack. Thus the middle grades of rice eaten by the Bengalis who suffer from epidemic dropsy are invariably parboiled and milled. As it is a cheaper grade proper preservatives are not added, so that the grain is very apt to get diseased if improperly stored.

Chemical tests.—It is well known that the cheaper rices are more indigestible but sweeter, as has been shown by numerous analyses. To illustrate this point we selected two samples of healthy rice and submitted them to Dr. N. L. Bannerji for chemical analysis. which he kindly carried out for us. The results were as follows:—

Name of the Rice.	Kjeldahl.	Protein % = N X 6·25.	Amino N. * Van Slyke.	Crude Fibre.	Cane Sugar.	Reducing Sugar.
Burma Rice.	1·001%	6·25%	0·935%	0·63%	0·08%	0·02
Dadkhani Rice.	0·966%	6·03%	0·91%	0·22%	*nil*	trace.

* Van Slykes, estimation of amino nitrogen was performed after complete hydrolysis of the rice by means of 20 per cent. HCL and the solution was afterwards practically neutralised and acted upon by HNO_2 for 5 minutes with shaking.

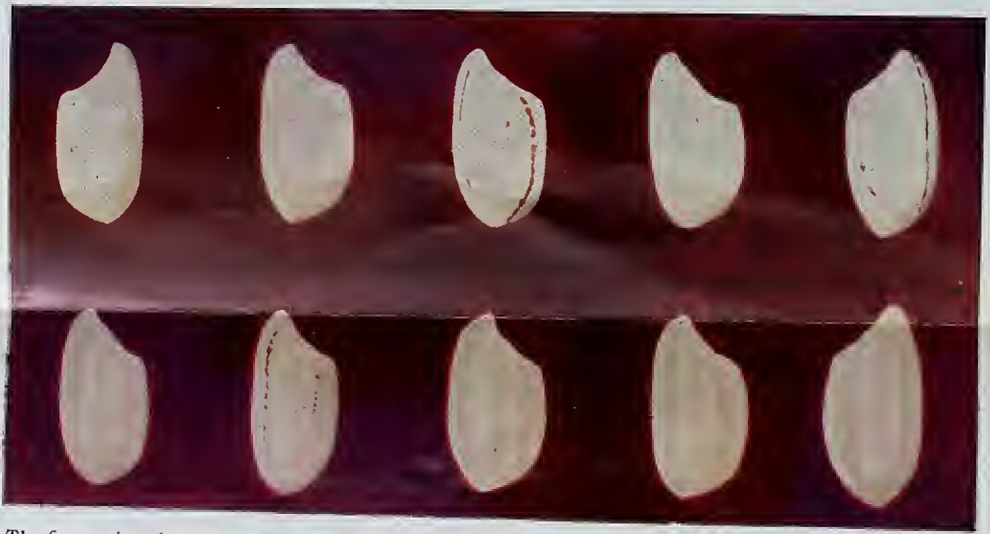
It will, therefore, be seen that the Burma rice contains more crude fibre and more sugar than the *dadkhani,* a good grade rice.

DISEASED RICE.

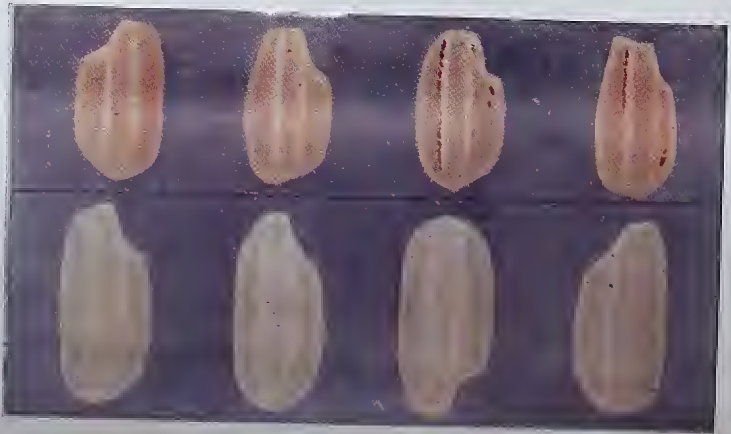
When rye is infected with *Claviceps purpurca* the grain turns a black colour and the diseased grain can readily be made out. With rice on the other hand, the colour is not altered but the grain becomes opaque and this is not noticed by the ordi-

PLATE I.

Showing the appearance of healthy and diseased rice by the water test.



The five grains above are diseased Burma rice and the lower, healthy rice. In polished grain the attack may come from the surface.



Burma rice, healthy, yellow and horny in appearance.

Middle grades, waxy in appearance.

nary individual. To detect this diseased rice the following tests have been employed by us:—

(1) The water test.
(2) Section of the grain.
(3) The chemical separation of the water,—and alcohol-soluble bases.
(4) Pharmacological tests.

(1) *Water test.*—(Plate I). Amongst people whose main food is rice, it is astonishing how few of them are able to recognise diseased rice. Amongst the various medical men to whom we have shown this test there was not a single individual, who had seen it used to test the condition of the rice. We are indebted to a rice merchant for showing us the test, which is employed by the trade. The test is simple enough, and consists merely of throwing a small quantity of the rice into a glass or brass dish, which contains water and then looking at the various characters and defects of the grain. If the grain is allowed to stand too long in the water, the fruit becomes swollen and opaque, but this takes some ten ninutes or more, so that there is ample time to study the rice.

The first character to look at is the size of the grain; the coarser rices are short and plump, and the medium grains longer and thinner, whilst the best grains are generally rather long and fine. The coarser rices have a horny appearance, the medium and finer grades are waxy in appearance, and the longer the seasoning the more waxy is the character of the grain. Fruit that has been for a long time stored in the husk or over-steeped is often tinged with a yellow or reddish colour. Again one can easily see whether the rice has been polished or unpolished by the presence or absence of the sub-pericarpal layer.

(*a*) When the fruit is diseased the grain becomes absolutely opaque. In coarser rices the colour is slightly yellow, whilst the medium grains have a dead white plaster-like colour. In the polished rice, the invasion may be from the surface of the grain, or from the embryonic site. In parboiled unpolished rice the attack is usually from the embryonic side. The grain may be attacked by various fungi which will be described in detail later, but for the present we will only consider bacterial infection. This usually occurs from the embryonic site, or through injuries inflicted during the polishing processes of the grain. Under these conditions the disease of the grain is not so easily recognised unless this water test is used to demonstrate the increase in the opacity of the grain.

(*b*) Fungi attack the rice during the monsoon months of July, August, and September, when the temperature is lower but when there is a high humidity present which makes everything damp, e.g., leather gets attacked by a brown, yellow or black Aspergillus, the same happens to the rice grain if it is damp, and becomes yellow or brown in colour but the fungus does not invade the grain, and when the grain is attacked the rice merchants in order to avoid a loss repolish the rice. During this brushing process the grain, being more friable, is apt to break into small fragments or blocks, and these are technically known as brushings. The brushings are mixed with healthy grain, and sold to the public. This simple test tells us the character of the fruit, whether polished, unpolished, healthy or diseased, or whether it is mixed with brushings.

In all the cases where we have been able to test the rice actually eaten by the affected epidemic dropsy families, the larger portion of the grain has been attacked by this bacterial disease. In some families we failed to find any infection of rice, as they only bought small quantities at a time from the retail merchants.

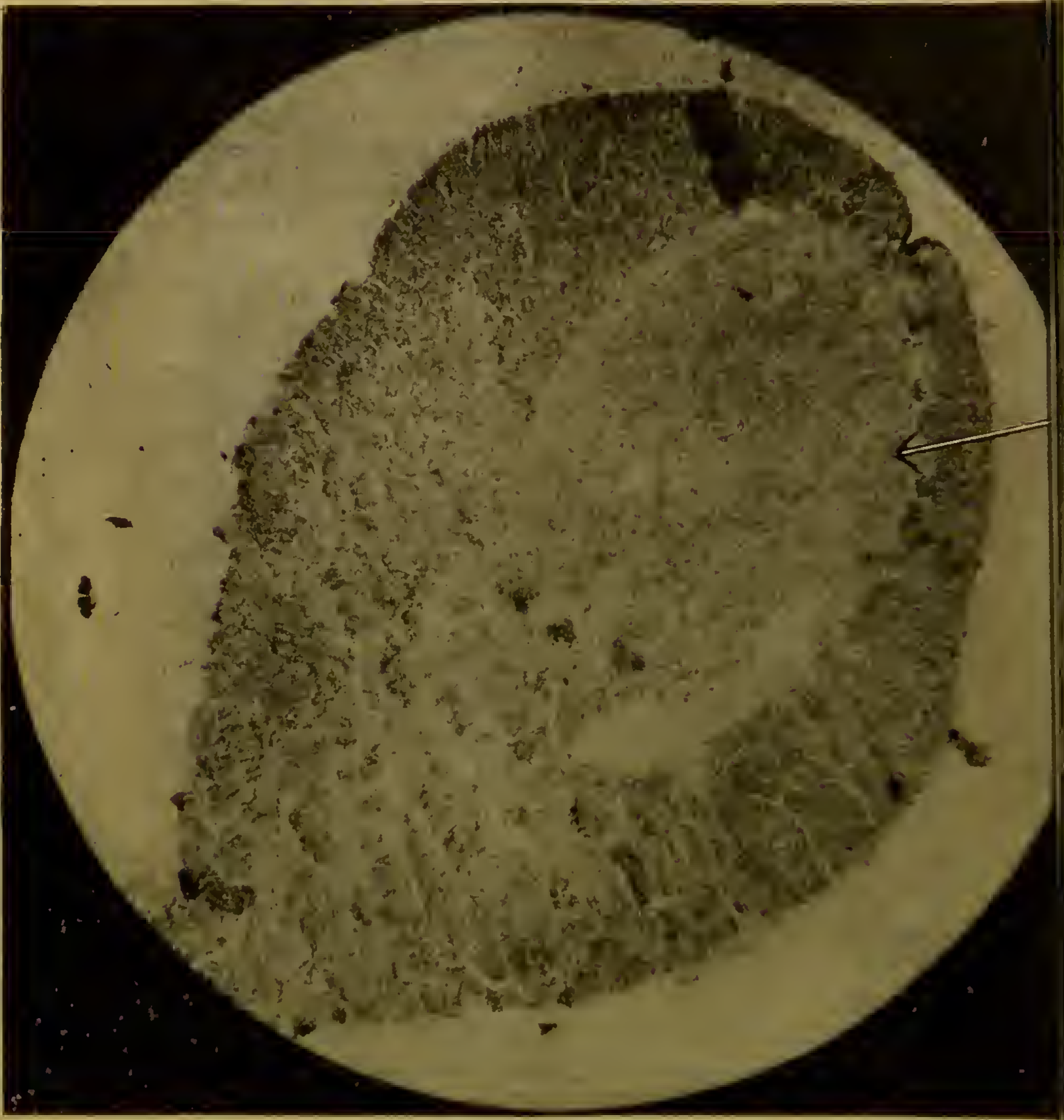
In some samples of rice kindly sent to us by Major J. Jolly, I.M.S., from Burma suspected of producing beriberi in jail populations, one sample consisted of a medium grade rice which was unpolished, but was extensively adulterated with diseased coarse grain Burma rice; the other samples were Burma rices in which almost every grain was found to be diseased.

(2) *Sections of the rice with white opaque grains, show a liquefaction of the starch cells* (Plate II). This liquefaction may commence from the surface in polished grains or from the embryonic site. It is, however, necessary to differentiate this from the burrows of the larvæ of weeviles. When the grains are badly diseased, the rice can be crushed up into a fine powder by the fingers. In future we will speak of such grains as diseased rice, and where no such change can be seen as healthy rice.

(3) *Chemical separation of the bases from diseased rice.* In every experiment we carried out on diseased rices, we used the water test to see whether the grains were really diseased or not, and the rice was always obtained from the actual food supply of infected patients. We also tested a sample that was obtained in the market similar in quality, but not showing disease by the water test: this acted as our healthy rice bases, i.e., as control. In cases where we obtained rice which appeared quite healthy and obtained from persons suffering from epidemic dropsy, we found that the original stock had been exhausted and this sample was from a new source of supply. During the last three years of experience on the extraction of these bases from diseased rices, our chemists—Mr. N. R. Chatterji, M.SC. and Mr. A. T. Dutt, B.SC.—now employ the following processes,

and we may here take the opportunity to express our thanks for all the work and energy they have expended on this research. Without their co-

PLATE II.



(1) Microphotograph of a section of a diseased rice grain—showing the area of lique

operation we would have been still in the blind stages of feeding animals on polished and unpolished rices.

The bases extracted can be divided into two categories—

(*a*) Water-soluble bases.

(*b*) Alcohol-soluble bases.

(*a*) *The water-soluble bases* were extracted as follows:—One kilo of coarsely powdered rice is soaked in a litre of water and kept overnight in the cold room at 4°C. Next day it is filtered and treated with the same bulk of water and this is repeated three times, the filtrates being kept in the cold room to prevent bacterial changes. A sufficient quantity of sulphuric acid is added to the total filtrates to make it a 5 per cent. solution. The bases are next precipitated with phospho-tungstic acid and filtered. The precipitate is washed and dissolved in diluted acetone (two parts of acetone to 3 parts of water) and then decomposed by baryta water and filtered. The barium is removed from the filtrate by CO_2, and finally any trace is precipitated by a few drops of sulphuric acid. The solution is then filtered and neutralised by dilute sodium carbonate. Then evaporated to dryness under vacuo. This constitutes the total water-soluble bases from epidemic dropsy or beriberi diseased rices.

The total bases are then fractionated in the following ways:—

(*i*) They are dissolved in weak sulphuric acid, and precipitated by silver nitrate. This precipitate constitutes the purine fraction and the silver is removed by dilute hydrochloric acid.

(*ii*) The filtrate from the purine fraction is treated by an excess of silver nitrate and a few drops of baryta added when a brown precipitate occurs, the histidine fraction. The metals are removed from the precipitate by hydrochloric and sulphuric acid.

(*iii*) The filtrate from the above is now treated by an excess of baryta and a further precipitate occurs, "the argenine fraction." The barium is removed by sulphuric acid.

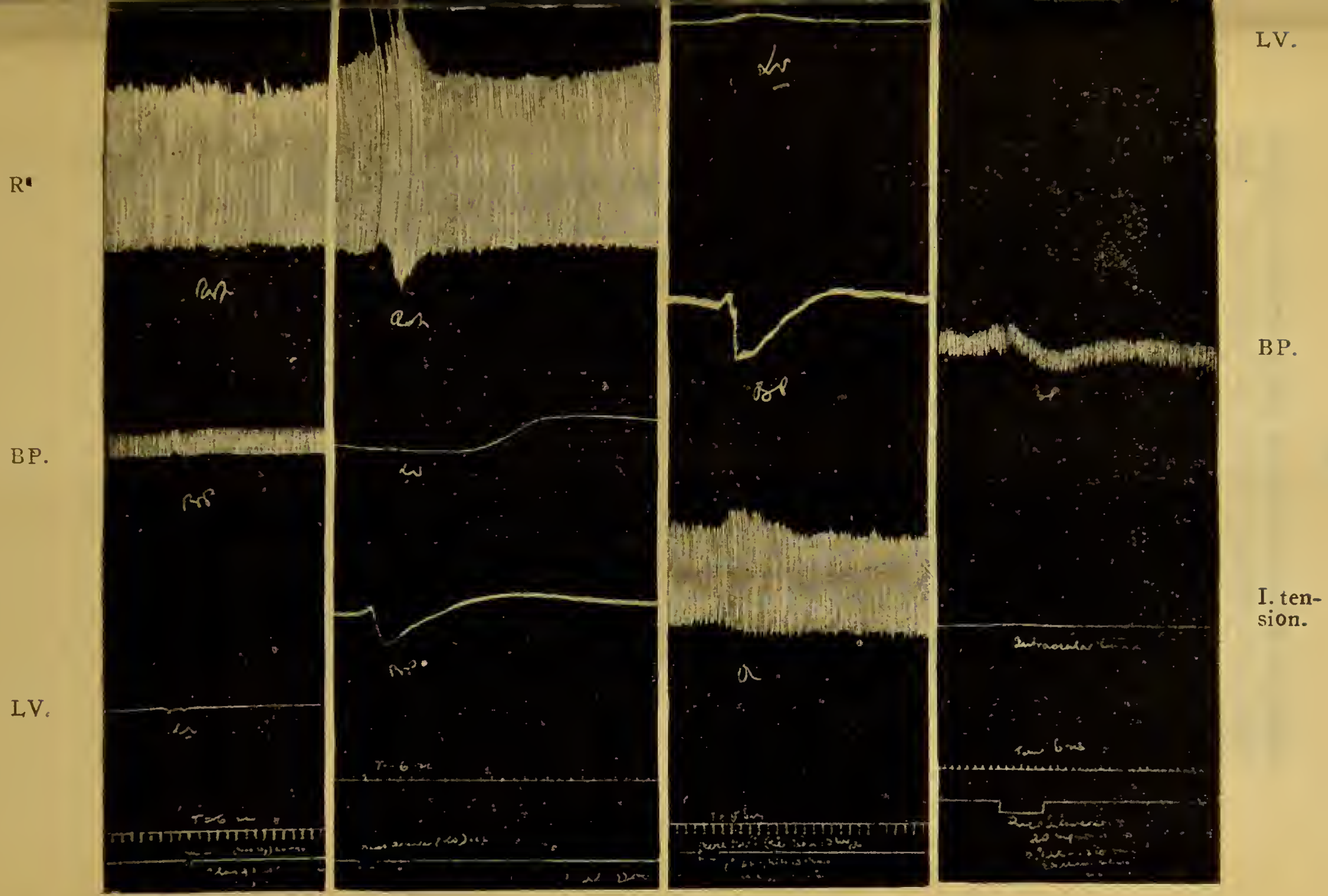
(*iv*) The solution from the above is made free from barium by blowing CO_2 through the solution and then by a few drops of dilute sulphuric acid, and any trace of silver by hydrochloric acid. The filtrate is evaporated to dryness in a vacuum, "the lysine fraction."

(*b*) *The alcohol-soluble bases.* The crushed rice was soaked with rectified spirit in a percolator for 48 hours. The extract was then drawn off and the alcohol recovered by distillation. The residue was extracted with petroleum-ether to remove fats and oily matter. Then rubbed in a mortar with absolute alcohol and was then filtered, and the alcohol removed by evaporation. The residue was dissolved in dilute phosphoric acid and utilized for tests.

These bases were then submitted to pharmacological tests.

(4) *Pharmacological tests.*—Graph IV shows the effects pharmacologically obtained from the total water-soluble bases of the different rices : (*i*) From healthy rice there is no effect seen. (*ii*) With the bases from epidemic dropsy rice, showing marked bronchial constriction, a slight fall in blood pressure followed by recovery, but the important point to notice is that there is a marked rise in limb volume which is delayed and is not due to a vascular dilatation. (*iii*) Shows the effect of the bases from beriberi rice; here the bronchial constriction is much less marked, and the limb volume rises only as a result of the general vaso-dilation, which is consequent on the fall of blood pressure. (*iv*) The intra-ocular tension with the bases from epidemic dropsy rice (shows a slight rise). Colonel Coppinger who kindly examined ophthalmoscopically six cases, that were recently under our care, noticed marked cupping of the disc in all the cases. Graph V shows the effect of the lysin fraction of the bases of beriberi rice on the excised heart of a rabbit. There is at first a very marked augmentation of the heart beat, which is soon followed by a diminution of the beat, and in a very short time the heart almost ceases beating.

Graph VI shows the effect of the alcohol extract of epidemic dropsy rice. In the alcoholic extract there is a bronchial relaxor, which causes a great



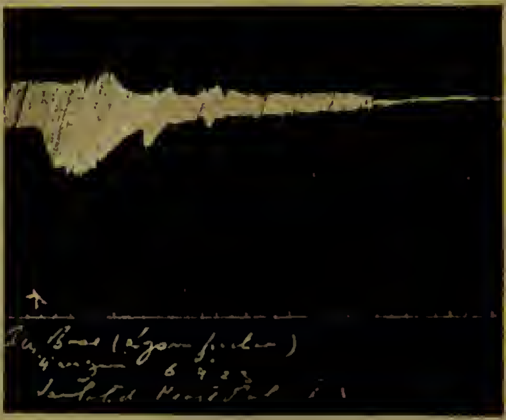
Healthy rice. Rice of epidemic dropsy. Rice of beriberi. Rice of epidemic dropsy.

LV.=Limb volume. BP.=Blood pressure. R.=Respiration. I.t.=Intraocular tension.

augmentation of the heart beat; the limb volume rises and remains raised for some time. The lysin fraction of the water-soluble bases contains a substance which causes bronchial constriction, a marked rise of blood pressure which is sustained, and a rise in limb volume following more slowly after the rise in blood pressure.

GRAPH V.

Showing the effect of the bases from the lysin fraction (beriberi) on the isolated heart.

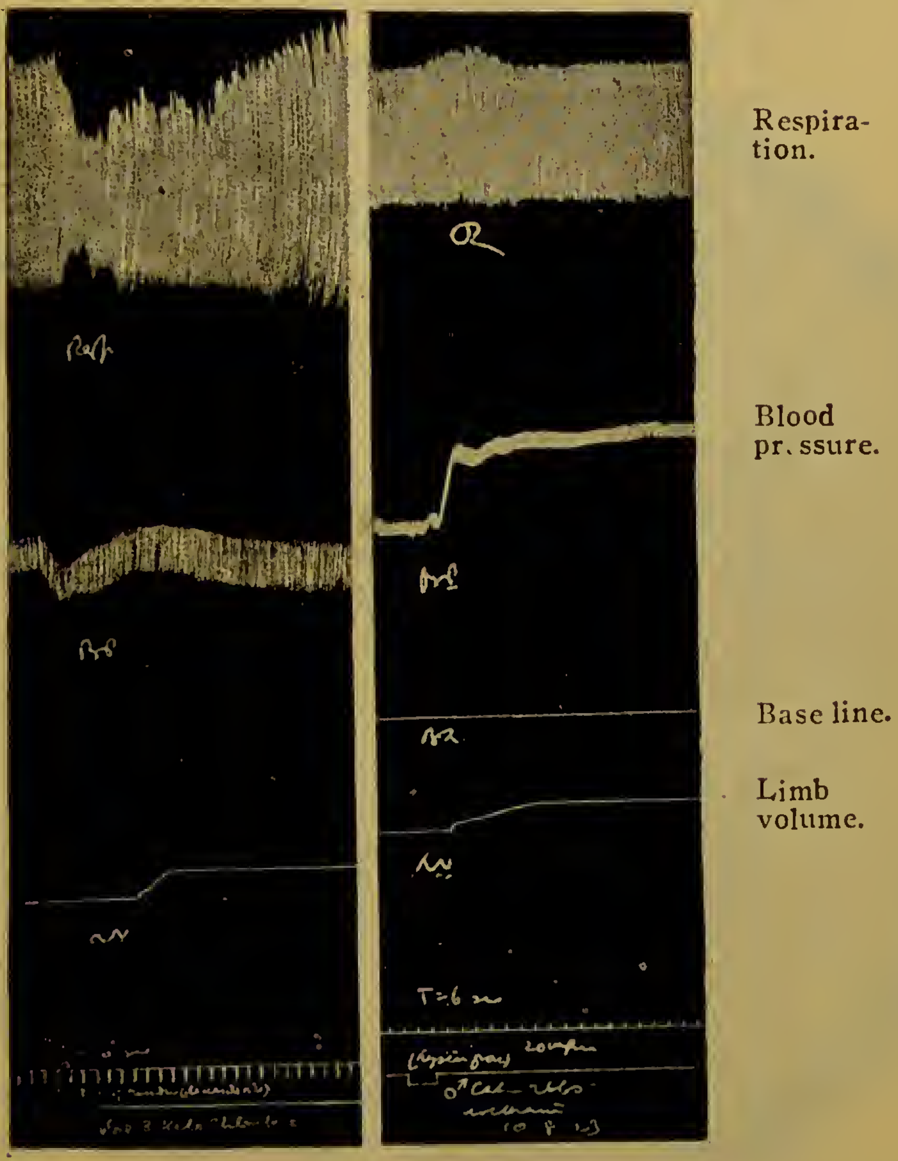


Lysin fraction (beriberi rice).

Graph VII shows the effect of the bases obtained from beriberi rices. (*a*) Shows the effect of the histidine fraction: here we have a bronchial constriction effect, a fall of blood pressure, and no alteration in limb volume. (*b*) Shows the effect of the lysin fraction: here there is a very marked and sustained rise of blood pressure, a marked relaxation of the bronchial muscle, a marked rise in intestinal volume and movement: in spite of the rise in blood pressure, the limb volume is not altered. (*c*) Shows the normal effect of pilocarpine on blood pressure and respiration, i.e., a fall of blood pressure and bronchial constriction. The bases obtained from the alcoholic extract of beriberi rice completely inhibit the effect of pilocarpine.

GRAPH VI.

The alcohol and lysin fraction of epidemic dropsy rice.



Alcohol extract. Lysin fraction.

We have therefore in these rices the following pharmacologically active bases. The total water-soluble bases from epidemic dropsy rice produce bronchial constriction and a rise in limb volume and this effect is not seen with the water-soluble bases from beriberi rice.

In the water-soluble fractions the active bases are as follows:—

(*a*) Histidine fraction, more marked in epidemic dropsy rice, a substance like histamine which causes a fall of blood pressure and marked bronchial constriction.

(*b*) Lysin fraction, more marked in beriberi rice; a very powerful base which causes a rise of blood pressure, bronchial relaxation and on the excised heart, first stimulates and then arrests the heart beat.

In epidemic dropsy rice there is no bronchial relaxation and there is a rise in limb volume.

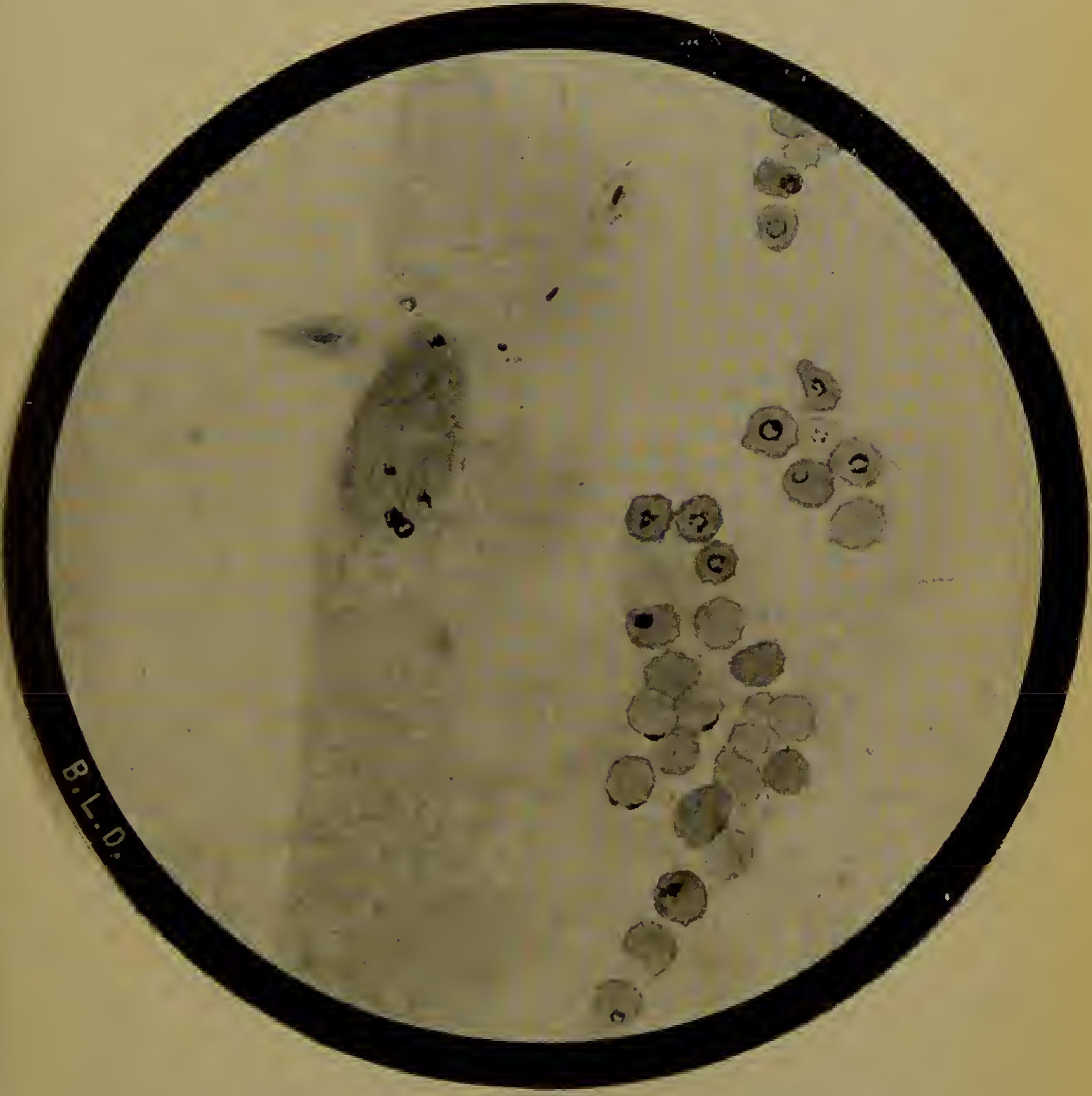
In the alcohol-soluble bases:—

(*a*) Epidemic dropsy rice bases augment the heart beat, cause bronchial relaxation and a rise in limb volume.

(*b*) In beriberi rice there is no effect on respiration or blood pressure, but paralysis of the parasympathetic as shown by the blocking of the normal action of pilocarpine.

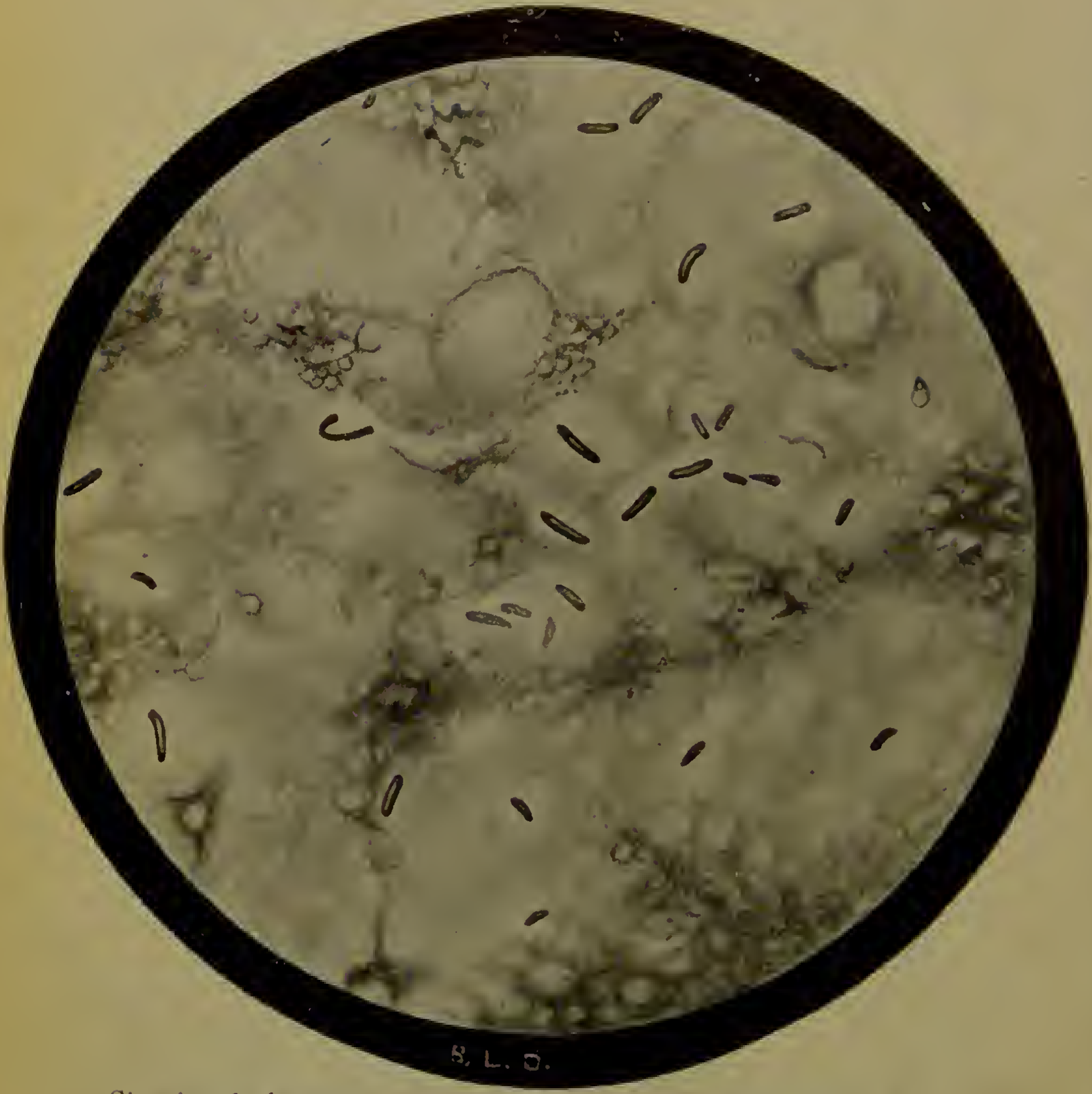
You can now realise our first difficulty when we had these varying reactions to contend with in these diseased rices, as we had not realised the difference in their end-decomposition products. These bases are sufficient to explain the neuritis, gastro-intestinal, cardiac, and other symptoms of the two grades of rice; epidemic dropsy rice has more water-soluble bases producing œdema, whereas beriberi rice has more of the neurotoxin.

PLATE III.



Section of the grain stained with carbolfuchin showing the spores of a smut.

PLATE III.



Showing the bacteria in the liquefied area stained with methylene blue.

THE CAUSES OF DISEASE IN THE RICES CONCERNED.

We have already seen how the milling and polishing processes damage the grain and render it liable to attack at the embryonic site and from the surface when the rice is highly polished (*see* Plate I). There is another factor that sometimes helps in the disease of these grains, and that is the infestation of the rice by the larvæ of various weevils and moths.

To show the cause of the disease in the grain we adopted the following methods of investigation:—

(i) *Sections of the grain.*—The technique which we adopted was one of these two methods.

In the first, the grain was boiled in a 3 per cent. acetic acid for a few minutes, then put into acetone for ½ to 1 hour, dried, and then put into an aqueous solution of glycerine and kept in the incubator for 3 or 4 days until the rice grains were sufficiently softened for sectioning, transferred direct into the paraffin bath for 2 hours, and then cut. In the second method, the grains were put into cellulose acetate in acetic acid overnight, washed in dilute acetic acid and then in water for half an hour, transferred into 50 per cent. alcohol for 1 hour, then into absolute alcohol for 1 hour and finally to the paraffin bath for 2 hours.

Sections were cut and stained by Möller's method for spores, and counter-stained with Manson's methylene blue. We are indebted to Dr. S. Bose, Botanist of the Carmichael Hospital, Belgachia, for showing us the technique for cutting these grains of rice.

Sections of the diseased grain showed the constant appearance of spores and less commonly of bacilli inside the rice grains (*see* Plate III). Occasionally we encountered a smut of which the spores were seen at the surface of the grain.

(ii) *Cultures from the diseased grain.*—The technique adopted by us was to immerse the rice grain for half an hour in pure carbolic acid in order to sterilise the surface. The carbolic acid was washed away by absolute alcohol, and the alcohol removed by sterile water. The grain was then broken into two, and planted with the broken surface downwards on agar, and a growth obtained of a spore-forming aerobe. No growth occurred when an unbroken rice grain thus treated was placed on the agar; showing that the bacilli were lying inside the grain. We found that boiling in 40 per cent. formaldehyde solution at 58°C. under vacuo sterilised the whole grain; the same happens when 1 in 1000 HgCl. solution is used.

(*iii*) We next ground up both healthy and diseased rices and the flour from these rices on an agar plate. In the diseased rices we invariably found the presence of a bacillus of the *vulgatus* group which we will describe in detail later. In the healthy rice this bacillus was also very frequently encountered. Besides these bacilli, we almost invariably grew colonies of Aspergillus of green, white, brown and less commonly of the black variety: a Rhizopus, probably *orysae*, was less frequently seen, and still rarer a Mucor. In all the plates there were numerous colonies of yeasts.

The organism isolated had the following characters.—It was a bacillus about 2.7μ long and 1 μ broad with rounded ends. It was a spore former; the spore was central in position and did not bulge the sporangium. It was a Gram positive organism, and stained well with all aniline dyes. The spores retained the stain well by Möller's method.

Cultural characters.—It grew well in the presence of air as well as under anaerobic conditions, at blood heat, and at 50°C. It therefore appeared to be a facultative anaerobe as well as a thermophilic bacterium.

Colonel Harvey, I.M.S., has directed our attention to the possibility of its living in symbiosis with an anaerobe and we are very grateful to him for this suggestion. But at present we have not been able to verify this point by growing the organism from a single bacillus. On agar it forms a white dry wrinkled growth, and on potato a copious white growth. On serum agar it forms a white wrinkled growth and in 2 to 3 days the medium becomes liquefied; until finally the whole slope is digested. Gelatine stab cultures show a marked area of liquefaction. Solid rice media is liquefied in 2 to 3 days. Litmus milk at first turns acid and then white, owing to the formation of leucobases, and finally the casein is digested.

Sugar reactions.—No change in lactose and dulcite, but glucose, saccharose and mannite are made acid and then the litmus is converted into leucobases.

Relation to heat and chemicals.—Infected rice when boiled in sterile water for 1½ hour, and then inoculated on agar plates gives the characteristic growth of this bacillus, showing that the spores are not killed during cooking of the rice. The spores require a temperature of 115°C. for 10 minutes to be destroyed.

We have therefore an organism of the genus Bacillus belonging to the *vulgatus* group, which is found both in healthy and diseased rice, but it is present only inside the grain in diseased rice and not in the interior of the grain of healthy rice. It happens to have an intense proteolytic action, and is therefore capable of producing various decomposition products from the proteins of the rice grains. What we desire to make perfectly clear is that we do not claim specificity for this organism. What we have found is that the organism has been demonstrated inside diseased rice grains, and that it has an intense proteolytic action on rice proteids. Whether it is the *only* organism of this large group of spore-forming aerobes that can attack the grain and produce these poisonous bases, we are not in a position to state definitely. In agricultural bacteriology, many of the decomposition processes are commenced by aerobes and completed by anaerobes; whether such a symbiosis exists in the rice decomposition we as yet have not been able to discover.

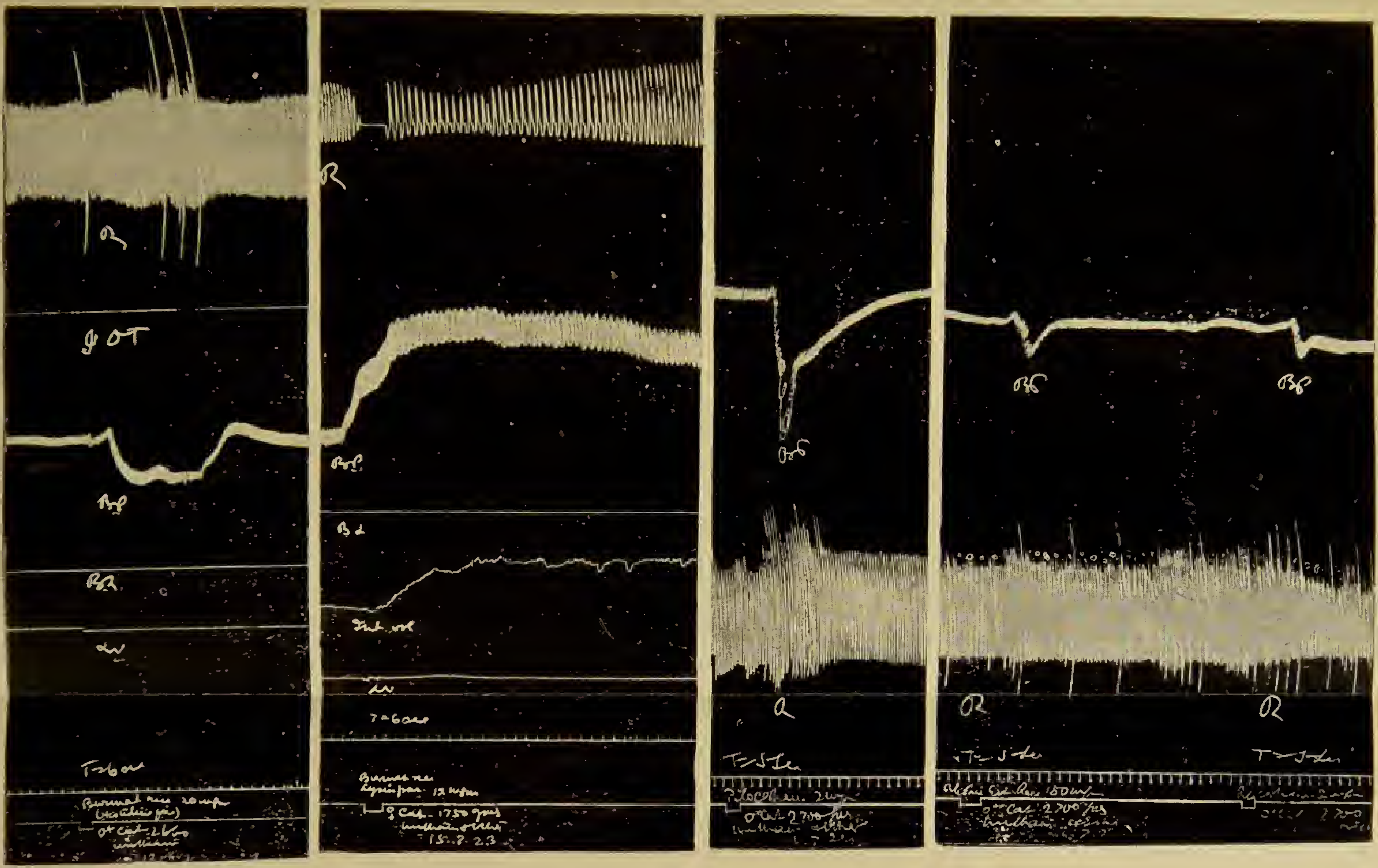
FACTORS INFLUENCING INFECTION OF RICE.

The rice merchants well know that rice is very apt to decompose in one of these two ways, depending on the moisture present in the grain—(*a*) If the grain has its ordinary moisture, it may become white and opaque, or (*b*) if it has been damped with rain, bilge water, etc., it is apt to become mouldy. The season of the year which is most favourable is during the monsoon months. If we study the meteorological conditions during this period, the results are shown in the following table:—

Month of year.	Air temp. °F.	Daily variations in air temp. °F.	Wet bulb °F.	Humidity%.
May ..	85·7	18·4	78·9	75
June ..	84·5	10·4	79·0	83
July ..	83·0	9·6	80·0	87
August ..	82·4	9·2	79·5	88
September ..	82·6	9·0	78·8	86
October ..	80·0	13·2	73·3	82
November ..	72·4	18·3	65·0	74

It will be seen that the most dangerous months are those of July, August and September, when the mean air temperature ranges between 82.4 and 83°F with an almost constant daily variation of 9°F and the humidity ranges between 86 and 88 per cent. saturation. This keeps the wet bulb temperature constant during the day and night between 78.8° and 80°F. The following experiments were devised by us to prove this point.

(*a*) Pre-monsoon period, during May and June when the air temperature was about 85°F with a daily variation between 12 and 18°F and the humidity about 75 to 78 per cent. saturation. Selected healthy rice was lightly sprayed with cultures of this *vulgatus* bacillus, and placed in glass dishes 4″ deep. One set was exposed to the air temperature and remained healthy, the other set was placed in a galvanised tank containing about 1″ depth of water and covered with a thick glass plate. The air here was well saturated and in a week's time every grain of the rice was attacked by this bacterial disease. From this diseased rice we were able to eaten by persons suffering from beriberi—the fractions obtained from the water- and alcohol-soluble.



Water-soluble histidine fraction.

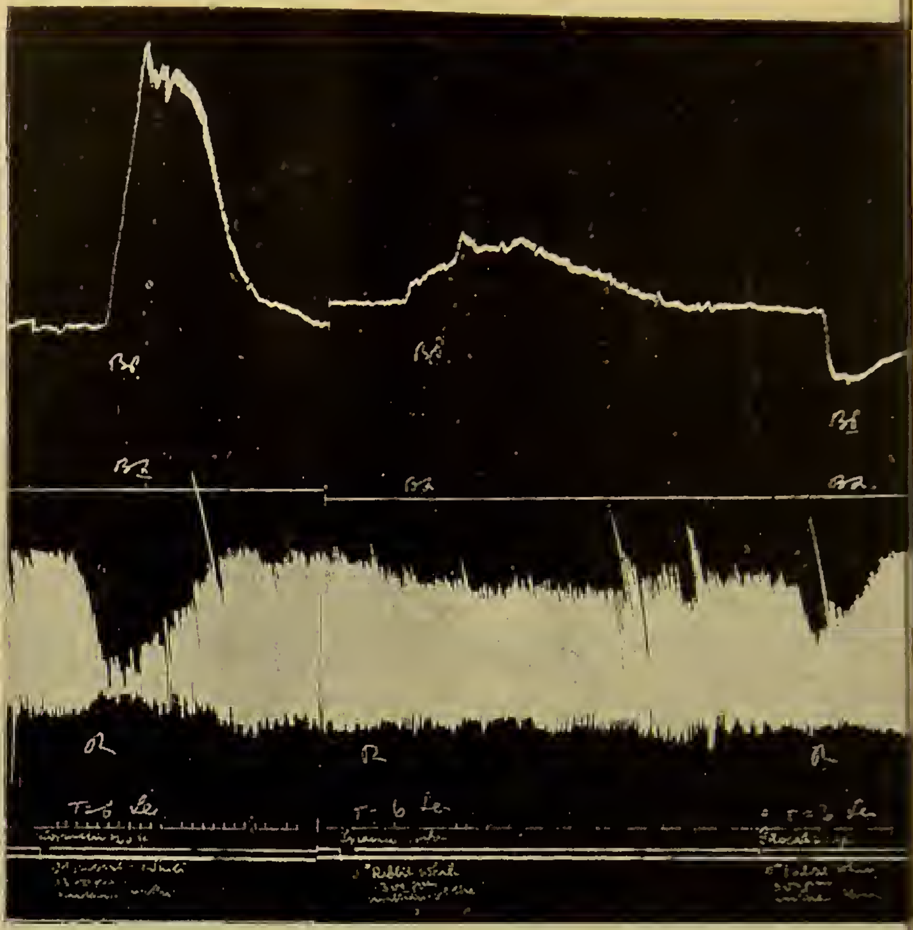
Water-soluble lysin fraction.

Pilocarpine

Alcohol extract of rice. Pilocarpine.
Paralysis of parasympathetic.

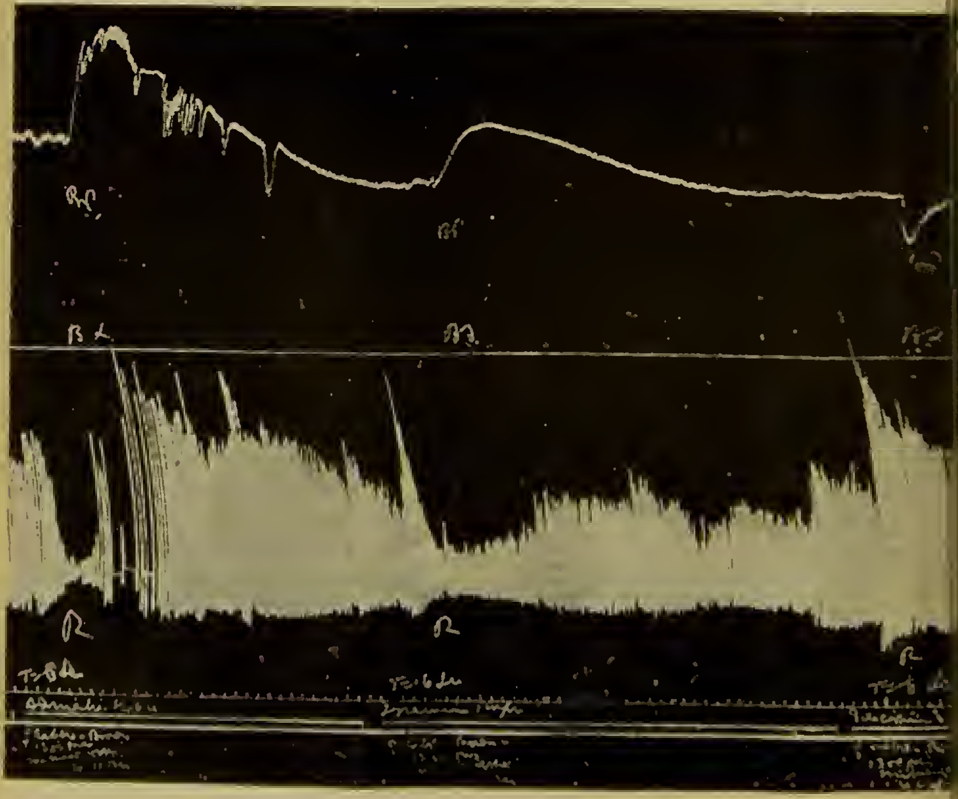
GRAPH IX.

Showing the relationship of colour to the intensity of action to certain b



Adrenalin. Tyramine. Pilocarpine.

WHITE RABBIT.



drenalin. Tyramine. Pilocarpi

BROWN RABBIT.

separate out the water-soluble bases in the histidine and lysin fraction and also the base that cause œdema.

(*b*) Monsoon-period, during July to September, when the humidity ranged between 86 to 88 per cent. of saturation. Of the rice trays exposed in the laboratory after spraying, all were affected by this bacterial disease. But on the other hand, the trays in the water tank were rapidly attacked by fungi, Aspergillus, Mucor and Rhizopus: these fungi did not invade the grain but altered its colour from a black to yellow, in a short time the grain became sodden and one could detect the odour of alcohol from the yeast fermentation.

(*c*) Post-monsoon, end of October and November, when the humidity had fallen to 82 to 74 per cent. of saturation. The rice in the trays in the laboratory remained healthy, but the ones in the saturated atmosphere were moderately attacked by this bacterial disease.

We, therefore, see that the main factors in causing this bacterial disease of rice are the constant high wet-bulb temperature day and night, only varying between 78.8 and 80°F in the 24 hours, and the intense humidity of the air between 86 to 88 per cent. of saturation.

THE ARTIFICIAL PRODUCTION OF THESE BASES.

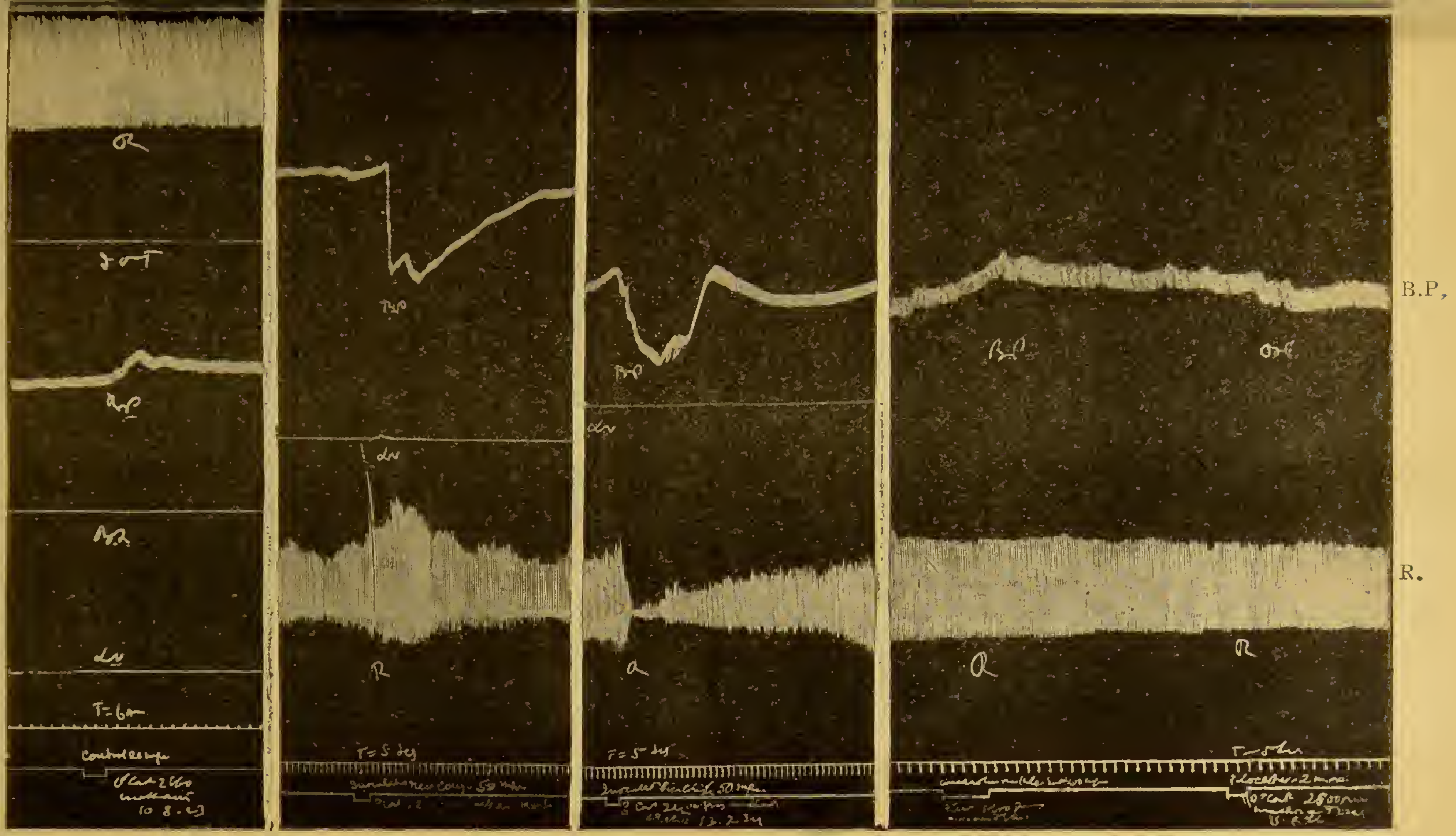
Until we could produce the various bases under artificial conditions we were not in a position to be certain of our results of this investigation:—

From cultures of the rice which had been artificially diseased by spraying it with this organism, and then keeping it under suitable conditions of temperature and humidity, we were able to separate these various crude bases. This test was not however sufficient, as we could not exclude the various other organisms that may have been present in the so-called healthy rice. In order to prove this point, we prepared rice media as follows:—

250 grammes of rice flour, made from medium grades and coarse grades of rice, were boiled for 1 hour in a litre of water. The volume was adjusted to 1 litre, autoclaved for 20 minutes at 115°C. to kill the spores, and then incubated for 2 days at 37.5°C. to prove that they were sterile. Uninoculated flasks were then incubated and kept as controls. The inoculated flasks were inseminated with this bacillus of the *vulgatus* group, and grown aerobically at 37°C. for 10 days. During the incubation the rice media which was solid to commence with was gradually liquefied, and by the third or fourth day was quite fluid. The controls and incubated flasks were treated chemically and the water-soluble bases extracted from them.

The results are shown in Graph VIII. We may point out that this graph is not the result of one observation but of several observations. We have been working on this disease since 1922, and these graphs are the selected results of three years of hard work. The first portion shows the results of 20 mgms. of bases from the uninoculated control. The second portion shows the effect of the bases isolated from inoculated medium grade rice. Here there is seen a histamine-like effect, marked bronchial constriction and a fall of blood pressure without any augmentation of the heart beat. In the third portion, an inoculated rice of a coarse grade, here the fraction in the lysin portion is more apparent, there is a marked fall of blood pressure but it is rapidly recovered from; the heart beat is augmented and there is marked bronchial relaxation.

Artificially we were able to produce the same toxins in the histidine and lysin fractions. For a long time however we were unable to produce the neurotoxin that paralysed the para-sympathetic because time after time these attempts failed



Healthy rice bases. Inoculated rice bases. Rice media aerobic. Alcohol extract. Anaerobic rice culture. Pilocarpine.

under aerobic conditions. We then changed the conditions, as soon as we realised the high temperature and anaerobic conditions produced in rice that was decomposing in storage. The flasks were inoculated with the same bacillus and grown aerobically at 37.5°C. for three days until the medium was completely liquified, then the surface was covered with sterile vaseline and incubated at 50°C. for seven days. The alcohol-soluble bases were then extracted from the controls and inoculated rice. The fourth portion of this graph shows the presence of a neurotoxin in the alcohol fraction, and it is able to completely block the action of two milligrammes of pilocarpine.

We have therefore been able to produce artificially the bases present in the histidine, lysin and alcohol-soluble fractions in sterile rice media artificially inoculated with cultures of the same bacillus, isolated from diseased rice. Further, they produce similar results upon inoculation into experimented animals.

INDIVIDUAL SUSCEPTIBILITY.

The third difficulty which we encountered during this work was the question of the individual susceptibility of our animals. For a long time we were extremely puzzled to find dissimilar results from the same sample of rice base; one day it would produce a very good effect from our point of view, whilst if tested to-morrow on another animal the same base would be almost devoid of effect. At first we were inclined to look upon these variations as due to alterations in the processes of extraction employed by the chemist, or to deterioration by light, etc., until one day we decided to test two animals simultaneously; when in one we got a very marked effect. whereas in the other the bases were almost devoid of action. This experiment showed that we were dealing with some individual factor in our animals, and this lead us to investigate these individual peculiarities. The results are embodied in a paper by Acton and Chopra (1924).

There are two primary factors involved in toxicity; (1) the amount of poison ingested; (2) the variations in the internal defence mechanism, on which to a large extent depends the production of symptoms. Thus if the amount of poison be large in amount all the individuals involved will be poisoned; e.g., the incidence of epidemic dropsy in a family where every member is attacked; this is purely a question of toxicity. But in a jail population, where only a few prisoners are attacked and where the whole population is eating an identical diet, we are dealing with the susceptibility of the individual, as the dose of poison ingested must be just under toxic limits for normal individuals. When we investigated what constituted this susceptibility, we found it was a very complicated mechanism, which was associated, firstly with the rate of absorption of the poisons from the intestine, then with the defence mechanism of the liver, which dealt with a certain amount of these poisons, and so regulated the concentration in the circulating blood.

Before the poisons can act on the different tissues their rate of diffusion into the tissues is regulated largely by the endocrine secretions. Thus conditions of hypo-adrenia and hypo-thyroidism are favourable for these toxins to exert their maximum effect. The converse condition of hyper-function of these two glands prevents these bases from acting on the tissues. When conditions of susceptibility are favourable large doses will cause the death of these individuals and smaller doses will produce symptoms in them, whereas normal individuals under similar circumstances will either not die, or escape the disease. During the course of our snake venom experiments, Acton and Knowles (1914) noticed that susceptibility was closely correlated with the colour of our animals, i.e., white goats were more susceptible to cobra venom than black goats. Again Bose and Acton (1924) showed that black rabbits showed a greater reduction of blood sugar after injection of insulin than white rabbits, and this in its turn was associated with the amount of adrenalin present in these animals. We are extending these observations to the action of these bases, toxins, etc., the results of which will be published by us in a separate paper shortly. In Graph IX we see graphically how important is this association. In the upper graph is the record of blood pressure and respiration of a white rabbit; we see that $\frac{1}{10}$ of a c.c. of 1 in 1000 adrenalin raises the blood pressure from 70 mm. to 180 mm., whilst tyramine and pilocarpine have lost their characteristic effects on the blood pressure and particularly on respiration. The lower graph shows a similar record made on a brown " Belgian hare " rabbit; here we noticed that the adrenalin effect is much less marked, as the blood pressure is raised from about 85 mm. only to 130 mm. whilst tyramine and pilocarpine have their characteristic effects both on the blood pressure and respiration.

It is therefore apparent that if one tested these rice bases on a light-coloured animal with a high adrenalin content, the effects would not be at all characteristic, whilst typical effects would be seen in dark-coloured animals with a low adrenalin content. These effects were very puzzling to us in the earlier days of this research when we were groping to find our way out through this maze of difficulties. Now, however, we know that when an animal—usually a dark-coloured one—gives a poor adrenalin response, the action of the bases to be tested will be typical. McCarrison in 1924 did not realise this factor when he was endeavouring to explain why the birds in his different experiments gave a different percentage of infection.

THE ROLE OF THE VITAMINES.

The work that has already been done on this subject is too sound to neglect, and for us to consider only the poisonous bases found in diseased rice. On the other hand we rather suspect that we are dealing with a partial association; that beriberi is caused by these poisons in the rice, but that their action can be antagonised by the vitamines in various ways which we will discuss presently. The experimental work on the value of vitamines in beriberi has largely been done on birds, pigeons, fowls, etc., which have been fed on polished and unpolished rice. Megaw (1923) showed from the post-mortem lesions, that avian and human beriberi were not identical diseases, as in the former atrophy of the heart occurred and in the latter hypertrophy and dilatation. Another point against these bird experiments is the fact that the proper food for them is seed or grain unhusked with plenty of grit in order to allow the gizzard to thoroughly powder the grain and prepare it for the digestive juices further down the alimentary canal. Now a bird kept penned in a cage without any access to grit, and fed only on polished rice is unable to finely grind up the rice, and must suffer from the effects of this lack of mechanical digestive process. Further it is not necessary to give diseased rice, for ordinary healthy polished rice will cause avian beriberi. These facts will combine to point out that avian beriberi is a disease due to the formation of poisonous bases formed from the rice in the alimentary canal of these birds, due to the result of the imperfect grinding of the rice in the gizzard, and possibly to the altered bacterial flora as the result of this indigestion. We have heard that a French worker Marchoux, (1920) in Indo-China is working on these lines and considers that beriberi is an intestinal infection and the poisons are formed in the intestine, which would be quite possible in avian beriberi.

We will now consider the rôle that the vitamines play in this disease. Sajous first hinted that one of the functions of the vitamines was to supply the precursors for the various endocrine secretions: this must be a pure surmise until the chemical composition of these antagonistic substances is known to us. We extracted the water-soluble bases from rice bran and tested them pharmacologically; *see* Graph X. This experiment was performed on cats; in one the total water-soluble bases were tested, and here there is marked bronchial relaxation, a rise of blood pressure with an increase in the force and amplitude of the heart beat; and a tendency to a fall in the limb volume, results which are distinctly antagonistic to the poisons in the rice.

In the second experiment, the bases were separated into the four amino-acid fractions, and in the lysin fraction a very powerful base was found which acts on the bronchiole muscles and blood pressure, and in spite of the high rise in blood pressure the limb volume was not altered at all.

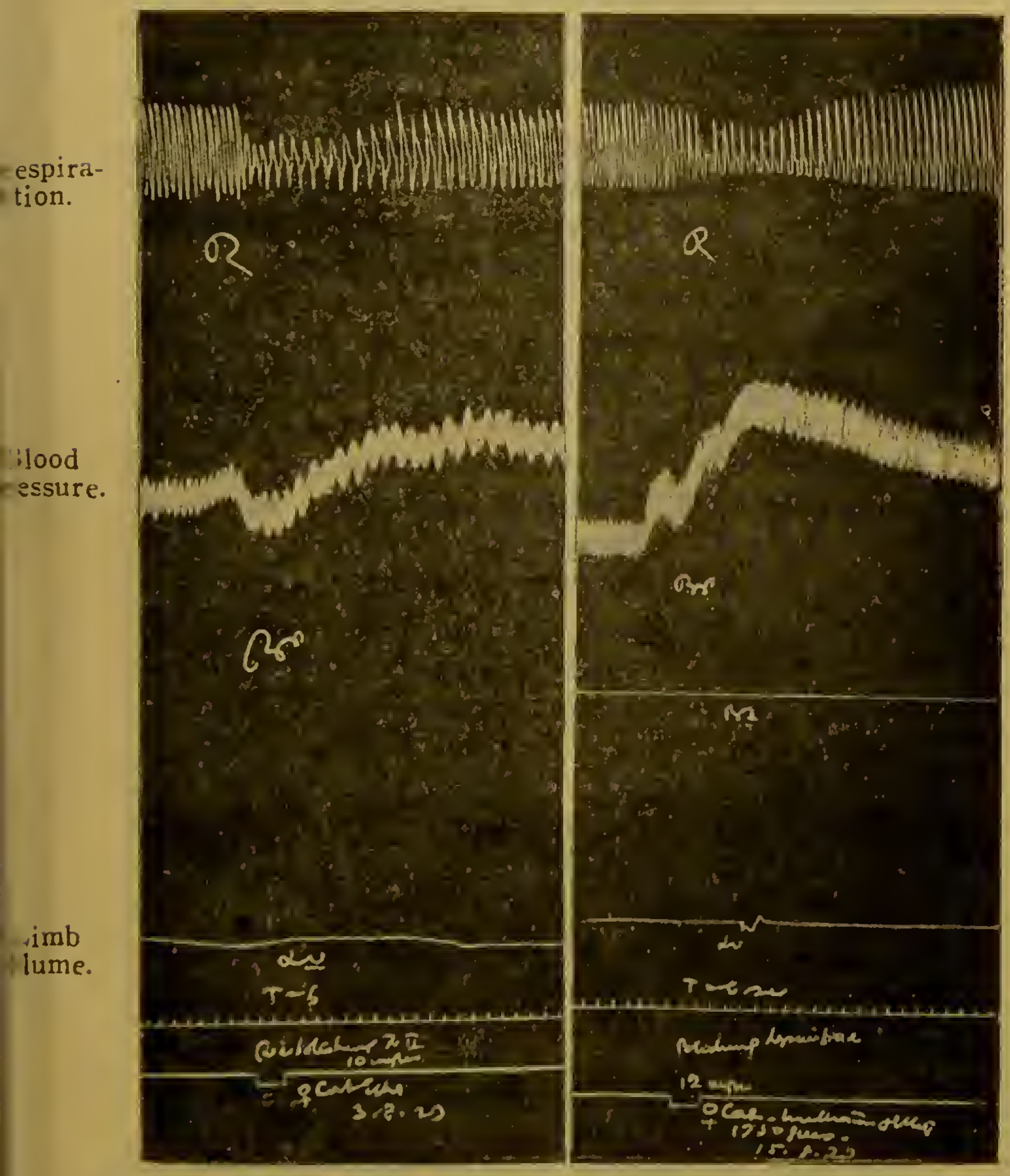
We therefore see that the pericarp of the rice acts in four different ways—

(*i*) Mechanically, by being impervious only to water and protecting the grain from invasion by extraneous bacteria and fungi.

(*ii*) The protective layer of bacteria. Professor Fowler of Bangalore has shown that in all seeds there is a layer of bacteria, specific

GRAPH X.

Showing the pharmacological effect of the bases obtained from rice polishings.



Total bases rice polishings. Lysin fraction rice polishings.

for the particular plants concerned, situated in the space between the pericarp and aleurone layer, and surrounding the whole grain. These bacteria prevent the ingress of extraneous bacteria that may possibly occur when the embryo ruptures the thinned out pericarpal layer over the embryonic site, during germination, and probably accounts for the increase in the vitamine content of germinating grain—compare hordenine in barley.

(*iii*) By virtue of these antagonistic water-soluble bases, anti-beriberi vitamines that are probably produced as the result of this bacterial action in healthy grain, especially if the bacteria are rapidly multiplying during germination.

(*iv*) In birds the husks and pericarp are required for the mechanical grinding that occurs in the gizzard.

Whether these vitamines are the sources of supply of such essential endocrine secretions as adrenalin, thyroxin, etc., remains to be proved as yet. But there is little doubt that with starvation or malnutrition all these secretions are diminished, and with a liberal diet of fresh foods, these secretions are brought up to the normal limits of health. The essential factor for the production of beriberi or epidemic dropsy is the presence of toxins in diseased rice, the pericarp and its vitamines preventing these diseases either by preventing disease of the grain, or by virtue of the antagonistic substances present, or produced in the body.

Feeding Experiments on Monkeys.

The lack of animal accommodation that we suffer from at this School, and the difficulty of obtaining a sufficient quantity of the diseased rice prevented us from carrying out any large series of feeding experiments.

(*a*) Two monkeys were fed on boiled rice from a specimen of rice obtained from an epidemic dropsy case. The water was dried by cooking. Both monkeys developed diarrhœa in 8 days and showed signs of anæmia on the 15th day. Œdema of the feet commenced on the 19th day, and on the 29th day one monkey showed distinct puffiness of the face and œdema of the wrists and feet; the other only showed the œdema of the feet. The experiment had to cease on the 41st day, as the rice supply gave out. These two monkeys were given two bananas each day with their feeds in order to supply vitamines.

(*b*) Two monkeys were fed on the same rice as (*a*) but the rice was well washed after the rice water had been thrown away. Two bananas were given to each daily. These two monkeys only showed diarrhœa on the 11th day, which soon passed off. They remained healthy till the feeding was stopped on the 41st day.

(*c*) Two monkeys were given boiled new rice with two bananas; they remained healthy up to the 41st day.

This small experiment means very little by itself, but it confirms our view that most of the poisons concerned with the production of symptoms in epidemic dropsy diseased rice are water-soluble, and the disease could be avoided to a large extent by washing the rice well after throwing away the *kanji* water.

TREATMENT OF THE DISEASE.

The first point we have to consider under this heading is the means which we can take to prevent these two diseases.

(*i*) *The use of the water test in areas where these diseases occur.*—It is an extraordinary fact that most of the foodstuffs eaten by man are seen or selected by women, yet how few of them know the quality of the foods they buy for their households. With European women, if it was not for the fact that meat was stamped 1st or 2nd class, not one in ten would be able to judge for themselves the quality of the meat their cook brings each morning. The same applies to the rice, the staple article of diet in Bengal; we can now recognise diseased rice without the water test, but doubt whether we would ever have discovered it without first being shown the test by a rice merchant. (By this test we can more accurately judge the quality, the amount of disease, and the presence or absence of brushings. In this way people could avoid buying rice that is dangerous to health.) For legislative measures on this subject, one should have the additional safeguard of chemical, and pharmacological tests.

(*ii*) *Proper Preservation.*—The public demand a highly polished rice, as it looks nicer, whilst the miller prefers parboiling as it is easier to separate the husks, so that the common rice in most markets is a parboiled highly polished rice, i.e., a nice looking rice which is cheap. The grain has been preserved as the result of past experience by the following methods :—

(*a*) The cheapest grades are usually not protected at all, but sometimes a little chalk is added to increase the white colour, and more rarely rice bran is added as well. All these rices are parboiled and polished.

(*b*) The medium grades, were in former days usually steeped and hand husked, but are now largely parboiled and always machine milled.

To each 60 lbs. of rice one lb. of rice flour and 4 oz. of lime is added as a preservative. The lime keeps the rice dry and prevents the excessive hydrolysis of proteids and any further hydrolysis of sugars by yeasts into alcohol, etc., as both organisms require a good deal of moisture. Many fungi require a minimum amount of moisture and so the hydrolysis of starches into sugars is attained by the addition of lime. The coarser grained rices have the highest sugar content, so the Marwari selects the cheapest grade of rice and has it seasoned by lime to meet his requirements at a minimum cost.

(*c*) The best grades of rice are always sun-dried or steeped and generally hand husked, and selected from the finer long grain of the *chotan aman* crop. They may be preserved for a long time, 10 to 15 years, e.g., *baspathi* rice in the following way, from the attack of insects, weevils and moths, by protecting it in gunny bags and by the addition of *neem* leaves. From bacterial action the rice is protected by keeping it dry by the addition of lime, arrowroot or rice flour, and turmeric which is considered to be an antiseptic.

(*iii*) *Storage.*—In Calcutta the dangerous time for rice to be infected is between the months from July to the end of September. Infection may occur immediately after milling, when the rice is stacked in large pyramids on the ground before being put into bags. The lower layer starts sweating; when bacterial change takes place the temperature rises and the rice gets damaged. Under these conditions the rice merchants repolish the diseased rice and mix it up with healthy rice.

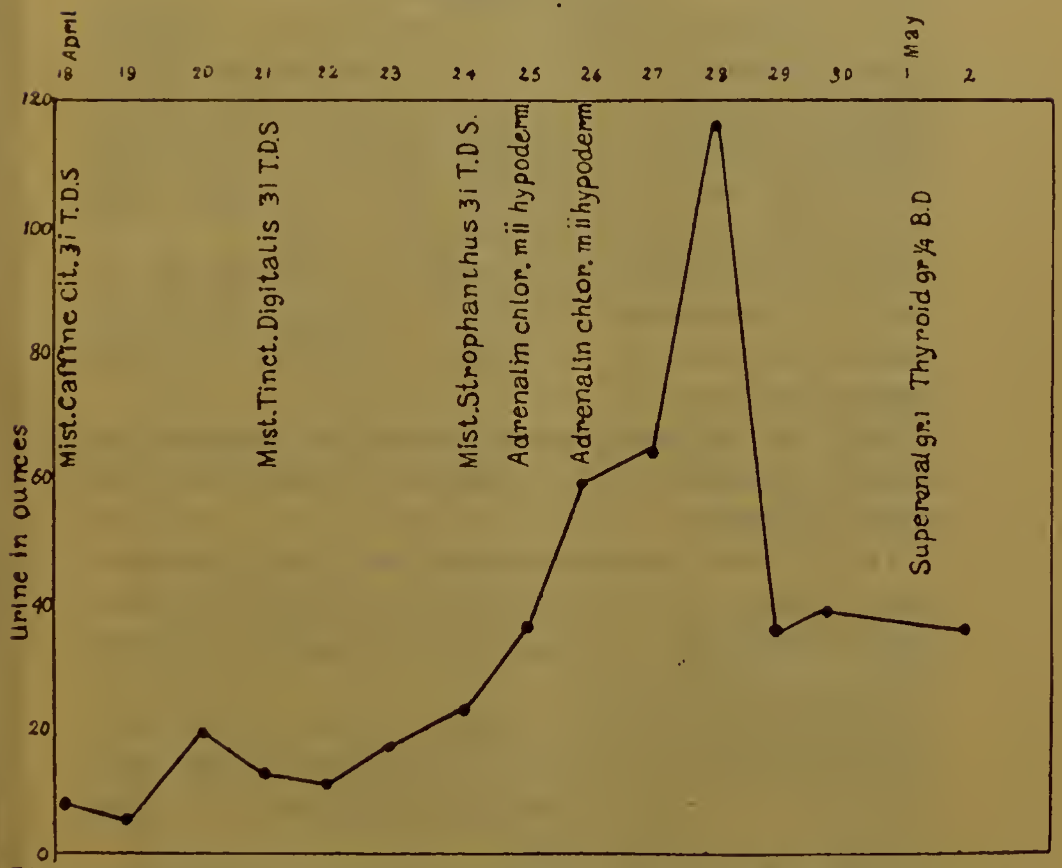
If the rice is stored in gunny bags and kept in cool ventilated godowns no infections will occur, but otherwise the lower bags will commence to sweat and disease occur. A similar condition occurs in ships when the rice is stored near the engine room and over the bilge.

(*iv*) *In rices causing epidemic dropsy* the bases are largely soluble. A careful washing of this rice is required, especially in large messes and communities like jails, etc. The neurotoxin in beriberi rice is not water-soluble.

(*v*) *The necessity for vitamines in rice and in the diet.*—As long as the public demand a highly polished rice and do not object to parboiling, so long will the millers supply this rice. Steeping the rice and lessening the polishing processes would do much towards the prevention of the disease in the grain. The absolute necessity for the different food-accessories (vitamines) is apparent from all the work that has been done on the subject.

Curative treatment.—The first essential is to remove the source of the poisons; it is therefore not necessary to stop the eating of rice, but to see that the rice supplied is not in any way diseased. The next essential step is to increase the general vitamine content of the diet, as many of these people are poor and have been subsisting largely on a rice diet with very few additions; a short time in hospital with rest and liberal live diet makes all the difference to these poor people. Our other experiments on susceptibility have shown the importance of adrenalin in blocking the action of many of these bases. It is the most valuable therapeutic agent which we have in this condition, as it stops the action of these bases, and diminishes susceptibility. It is not a miraculous remedy restoring nerves that have been damaged or heart muscle that has been badly injured: the subsequent cure of both these lesions depends on the extent of irremedial damage. Graph XI illustrates the value of

GRAPH XI·



Showing the amount of urine excreted by a patient suffering from beriberi and treated with caffeine, digitalis and then minims ii of adrenalin intramuscularly twice a day.

adrenalin in such a case where caffeine was first given, then digitalis, finally 2 minims of adrenalin intramuscularly twice daily: the urinary output suddenly rose, the œdema lessened and by the third day had disappeared. After a few days of the adrenalin injections, suprarenalin gr. 1 and thyroid extract gr. $\frac{1}{4}$ was given between meals, twice a day for three weeks, in the hope of diminishing the susceptibility towards these bases.

We finally have to thank Capt. P. De, M.B., Assistant Professor of Pharmacology for his invaluable help during the course of these experiments which involved three years' continuous work.

CONCLUSIONS.

(*i*) Epidemic dropsy and beriberi are different clinical aspects of a toxic syndrome caused by the ingestion of poisonous bases formed in rice under certain conditions; although similar poisons can be formed in other foods under storage; e.g., tinned provisions, dried fish, etc.

(*ii*) This disease in the rice can readily be detected by the water test, and moreover these two clinical entities are associated with two different grades of rice.

(*iii*) A spore-forming proteolytic bacillus of the *B. vulgatus* group is commonly found in such diseased grains.

(*iv*) These bacteria attack the fruit, particularly during the hot humid months of the monsoon, especially if the grain is stacked in non-ventilated rooms.

(*v*) Highly polished grain is more easily attacked owing to the loss of the aleurone layer and embryo, and the consequent exposure of the delicate cells of the fruit.

(*vi*) Parboiling kills the enzymes in the grain, and so further helps bacillary invasion.

(*vii*) Bacterial invasion of the rice occurs more commonly from the germ site, but in highly polished rice, it also occurs as commonly from the surface.

(*viii*) The bacteria and their spores, as well as their effects on the structure of the fruit, can be demonstrated by microscopical sections and cultural tests.

(*ix*) Experimentally by spraying rice or inoculating sterile rice media under certain conditions of temperature and humidity, the same poisonous bases are formed from the proteids.

(*x*) These bases pharmacologically produce all the signs of the disease; viz., œdema, heart effects, and para-sympathetic paralysis, and they are not present in the non-inoculated control rice media.

(*xi*) In sterile rice medium that has been inoculated by this bacillus under aerobic conditions at blood heat, the medium is liquefied and the water-soluble bases produced. The neurotoxin is only produced when the temperature is raised to 50°C. and the conditions made anærobic by a layer of vaseline.

(*xii*) The difference in the relative proportions of the signs in epidemic dropsy and beriberi is due to these bacteria acting on two different grades of rice, and producing different amounts of the toxins causing neuritis and œdema.

(*xiii*) The poisons in the rice causing epidemic dropsy are water-soluble and are therefore found in the rice water, thus explaining the incidence amongst Hindoo widows, and in large communities; in the former the rice is cooked till dry, in the latter it is improperly washed.

(*xiv*) The neurotoxin found in rice causing beriberi is soluble in alcohol only, so that the disease is seen in persons cooking for themselves.

(*xv*) Individual susceptibility plays an important part when the amount of poison ingested is small in amount, e.g., the small incidence sometimes seen in a jail population. When the quantity ingested is very large, e.g., in a whole family attacked by epidemic dropsy, it then determines the mortality.

(*xvi*) Hypo-adrenia in particular, and hypothyroidism to a lesser extent, increase the susceptibility towards these bases, and this in turn is closely correlated with colouration of animals.

(*xvii*) Rice polishings contain bases that are antagonistic to the bases found in diseased rice.

(*xviii*) The pericarp acts mechanically by preventing surface bacterial invasion of the grain, and is further aided by the protective layer of bacteria living under the pericarp of all fruit (Fowler).

(*xix*) Polished parboiled rice is the most dangerous of all rices and can be protected only by preservatives and proper storage.

(*xx*) Adrenalin in small doses, minims ii intramuscularly twice a day, diminishes cell permeability and so relieves the œdema, and also antagonises the action of the water-soluble bases. To a lesser extent it protects the para-sympathetic.

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IS EXCELLENCY THE GOVERNOR

P

OF THE STRAITS SETTLEMENTS

AND SCIENTIFIC POACHERS. 2

LONDON SCHOOL OF TROPICAL MEDICINE
LIBRARY

The Discovery of the Cause of Beri-Beri

Disease which has cost $9,000,000 and 100,000 lives!

ITS SUCCESSFUL PREVENTION.

It still costs a quarter-of-a-Million annually,
but may be prevented for nothing!

A Great Sanitary Reform needed *and a little Justice.*

BY

W. LEONARD BRADDON, M.B.,B.S., Lond., F.R.C.S., Eng.

AUTHOR OF

"The cause and prevention of Beri-beri." *

* Rebmans, London.

HIS EXCELLENCY the Governor of the Straits Settlements, in a recent Budget Speech made a statement the effect of which is to do serious injustice to at least one humble individual—the present writer.

His Excellency's remarks dealt with the question of beri-beri, the severe mortality it causes in the Colony, and the prospect of legislation being shortly introduced whereby the evil might be combated. That possibility—the possibility (if Government so choose) of complete eradicating a terribly frequent and fatal malady from our midst was due, said H. E.—was "the result" I think was the exact phrase—of work done at the Pathological Institute. Kuala Lumpur. Herein lies the burden of my complaint.

The implication that the discovery, whether of the cause of beri-beri, or of the means of preventing it, is the achievement of workers at the Institute is incorrect, and ill-founded—to put it bluntly, is

untrue.

A statement of the kind made by one in the exalted position of H. E.—the Governor of the S. S., and in regard to an important public service (such as all will admit the discovery of the means of prevention of a serious cause of mortality to be) could only have been due either to ignorance of the facts, or to a woeful want of candour in dealing with them, such as I should be loth to suggest.

But the misconception once engendered, the mistaken attribution once made, and thus unfortunately advertised by H. E.—perhaps not unsedulously fostered by those to whom maintenance of the illusion brings vicarious fame—unless early dispelled is likely to remain. I therefore propose to place the public in possession of the truth about a discovery of real public importance, and H. E. the Governor in a position to make amends for the no doubt unintentional injustice which he has committed.

Beri-beri

is not a matter of little or merely academic interest to this country. On the contrary, it has long been and yet indeed remains, through the amount of loss of life and work which it entails, a matter of very great economic as well as humanitarian importance to the Colony, and the Federated Malay States, and indeed all Eastern regions.

Last year, as Sir John mentioned in the speech referred to, over sixteen hundred deaths were registered as due to this cause in the Colony alone. In 1908 there were nineteen hundred deaths. In earlier years there were even more, the proportion being

one-fifth

of all the deaths registered, or about eight per thousand living annually—a rate of death from a single disorder which exceeds the average rate of deaths in England, for instance, from all the infectious diseases put together! A significant fact is, that the disease almost exclusively affects Chinese, whose proportionate mortality from it is thus far higher and more lamentable. The statement may hardly be credited, but is nevertheless well-founded, that of every thousand Chinese living 120 suffer from beri-beri in some degree, 80 are severely attacked, and 16 die of it annually. Most of these victims are young adults, otherwise healthy and vigorous and in the prime of life.

The experienced Medical Officer alone known how appalling are the the ravages of beri-beri. All over the country it steadily claims its victims, sometimes in holocausts. The writer has seen, at a mine, 200 healthy young labourers imported,

all

of whom were dead of beri-beri within a year. On an estate there were imported 80 Banjoerese from Southern Borneo.

Four were sent back

to Borneo less than a year later—the only survivors—the rest had died of beri-beri. On Christmas Island, which was the scene of an important commission of enquiry into the disease, with a population of only 700 individuals, there were in 1902 six hundred and ninety three cases (89 deaths), in 1903 five hundred and ninety one cases (60 deaths), in 1904 nine hundred and-seventy-three cases (91 deaths). During twelve years 1893 to 1904 there were treated in the Selangor State Hospitals alone 35,697 cases (deaths 6,624). In the Colony some 2,000 cases are treated in hospital every year. There have been treated in Government Institutions alone, during the last three decades, over

a quarter of a million cases of beri-beri

of whom **45,000 died.**

The total tribute of deaths during that period from this single disease in the Straits Settlements and Federated Malay States has been probably not less than 150,000.

Not only does beri-beri form thus the severest plague among the population at large, but continually in the past it has been a scourge of our public institutions, decimating or worse than decimating the unhappy inmates, supposed to be peculiarly under the public care, in the Asylums and the Gaols.

Thus in the

Singapore prison

from 1869 to 1882 the disease was never absent. The attack rate on the prisoners was enormous. Thousands suffered from it, hundreds died. The deathrate from it per thousand of the gaol population was never under, and often exceeded 24 per thousand. In 1879 it was 128 per thousand! During those 12 years the deaths of 463 individuals were ascribed and many more probably were actually due to beri-beri. Again in the 7 years following 1897 there were 1,582 such cases—83 deaths.

Remember, these unfortunates were inmates of a Government Institution, admitted able-bodied and healthy, only to acquire and perhaps die of an agonising malady. No doubt everything was done that could be done for them, *after* they had acquired the disease: but Government—Medical Science—was impotent to check the onset or hinder the course of the disorder—

for the cause of beri-beri was then not known.

In this Institution the malady continued its ravages till the end of 1904, when

a means of prevention

the only means of prevention—a single, simple remedy, profoundly simple, and even costless—the

writer's remedy,

had been discovered and applied.

The Singapore Lunatic Asylum

was from its beginning an even worse hotbed of the disease, and furnishes a still more painful history. Although the inmates averaged less than 200 in number between 1896 and 1901, for instance, the cases of beri-beri (and this includes only first attacks and not relapses, which were incessant) numbered 931 : the deaths numbered 231 ! In one year, 1898, the population being 208 individuals, 201 of them were treated for beri-beri, 55 dying ! The deaths from the horrible disorder in this Government Institution averaged 200 per thousand annually, or in other words the

whole population was destroyed

by it every 5 years. Here again everything that could be thought of was tried to check the spread of the disease, and relieve the unhappy inmates. But the efficiency of these attempts was *nil*—

the cause was still unknown.

Every endeavour to cope with the disease on the lines of infection (as it was then believed by the Superintendent and all other authorities to be) proved futile.

From 1902 onwards some amelioration took place. This followed the adoption, at first irregularly, but later in an efficient manner, of again the only remedy,—the single, simple, costless, but wholly efficient remedy, *the means of prevention devised by the present writer.*

In the Selangor Gaol (Pudu) and the Selangor Lunatic Asylum

the incidence of the disease had been hardly less disastrous. In the former, in the 8 years following its occupation in 1895, there were not less than 2,334 cases, many fatal. In the latter it was worse even than in the Singapore Asylum. Thus in the half year ending December 1898, 66 *per cent.* of the inmates were attacked ; in 1899, 94 *per cent*: and in 1905,

130 per cent !

Here once more the application of the remedy caused

instantaneous

and complete cessation of the disease, the Asylum becoming then freed from it for the first time in all the lamentable years of its history.

Of what nature was this remedy?

Placed by the present writer in the hands of Government, at a time when no other means of prevention of beri-beri was known, or even hinted at, when prevention seemed impossible and treatment hopeless; immediately utilised by them, with a success as instant and complete, as it has been (up to this moment) wholly

unacknowledged,

the remedy flowed naturally from the determination of the cause of the disorder, made and published by the present writer, before even the advent on the scene of those workers at the Institute of Research, to whom H. E. the Governor of the S. S., would now attribute the merits of its discovery.

Simple, inexpensive, claimed (and since demonstrated) to be a complete means of preventing a terrible and widely spread malady, and so long unknown!—it may interest the public to learn something of the steps of

the discovery of the remedy.

THE CAUSE of beri-beri (and equally of the means of preventing it) had long been the special medical mystery of the East, over which it has brooded immemorially like a cloud, sullen, fateful, fascinating, but insoluble.

Numerous Government Commissions, specially paid Expert Investigators had from time to time given labour to the research, in vain. Very many explanations, some entirely fantastic, had been offered as to the origin of the disease: and among them two chiefly found adherents. One was, that beri-beri rose from some sort of infection: the other, that it was the result in some way of bad food in general, or in particular of bad rice. Most investigators (all the supposed experts) favoured the former theory, and in the camp of its adherents were ranged all those who, having written books, were accepted as authorities on tropical disease. The advocates of the food—including rice-theories had always been few, and perhaps never very clamant. Their views, and the data by which they supported their conclusions, more or less carefully examined by those who led medical opinion (or formed it in the schools) had been weighed and found (by those authorities) wanting. I need not now go far back in the medical history or cite many names. There have been at least

a thousand monographs

written about beri-beri! But I will content myself with stating the pronouncements of the two best known living authorities on tropical medicine as stated in their publications. Professor SCHEUBE, the author of the most complete monograph of beri-beri, and also of one of the best known text books on Tropical Diseases generally, states dogmatically (Ed. 1900) "*beri-beri is an infectious disease.*"

SIR PATRICK MANSON, an original investigator of deserved repute, Medical Adviser to the Colonial Office, and author of the best known British text book on Tropical Diseases, after lengthy discussion of all the theories of beri-beri in various publications 1900 to 1903 rejected the food,—including rice-theories entirely. He plumped for infection—of some sort. These were the pronouncements of the authorities in 1900, and I see that in their most recent editions their opinions remain unaltered.

But in 1901 the writer published *facts* which made it practically certain, and in 1904 an accumulation of evidence which made it

absolutely certain

that, contrary to the views of the experts, beri-beri was not in any sense an infection, but a form of

food poisoning,

of which the cause lay in the nature of the grain, the cereal food eaten, the source in this country being the staple food *i. e.*,

rice.

It was shown—

1. That in places and in communities where rice-eaters* and non-rice-eaters lived side by side, sharing in common the chances of supposable infection,

beri-beri attacked invariably only the rice-eaters, never the non-rice-eaters.

2. That *among rice-eaters*, otherwise equally exposed to infection, *beri-beri again attacked those only who ate certain sorts of rice*, or rather rice

in a certain condition.

Those who ate fresh rice (as prepared by the Malays *i. e.*, hand pounded daily for their own use) and those who ate rice prepared by the parboiling process (as customarily used by Tamils, which I called "cured" rice) never got beri-beri.

It attacked those only whose staple diet was the common commercial white rice of the shops, the so-called Rangoon, or Siam rice—sorts which, in contradistinction to the other varieties, I designated "uncured."

3. That *the severity of the disease* and its extent (the number of attacks) in communities *was directly proportional to the quantity of rice consumed*. Its progress, whether as a malady of the individual, or as an epidemic in communities becoming greater when the rice was increased, diminished when this was lessened, and ceasing altogether when the noxious rice was withdrawn, without change of any other circumstance.

Let the reader carefully weigh these statements and consider whether, if true, they could be explained away by any conceivable form of infection? Or whether any conclusion can be drawn from them, other than the writer's conclusion, *i. e.*, that it is to the consumption of the incriminated rice that the disorder is due?

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* A rice-eater in this connection meaning not any one who at any time eats a little rice, but one whose staple diet is of that grain; conversely a non-rice-eater is one whose staple is usually of some other sort.

Accepting the data, it is demonstrated that beri-beri attacks only the users of a certain sort of rice: those who eat no rice, those who eat only cured rice, or fresh rice, are absolutely exempt. In other words ***uncured rice is the cause of beri-beri; and there is no escape from this conclusion, unless it can be shown that the data, the statements upon which it is based are untrue.***

The weight to be attached to a conclusion such as this depends largely on the ***extent*** of the evidence by which it is supported.

Had the demonstration been made in regard to one instance, one place, or one time, or in respect to a few persons only, it would have been remarkable. But the facts—the records proving them—referred not to one place or one country only, but to

every part of the country

every state, every town, village and hamlet, every mine, plantation or settlement, throughout the Native States and Colony, wherever the material, the native races, thus subject to or exempt from the disease, lived beside each other and were under observation. They were noted not in one year only, nor at one particular season, but throughout

every season of every year,

and during all the thirty or more years that the country has been under medical observation.

They referred neither to few communities, nor to small numbers of individuals, but to

every community

every one of the thousands of communities into which the population is divided, and to numbers of persons aggregating hundreds of thousands.

The records comprised not only the writer's personal observations, but those of his colleagues in charge of the forty or more Medical Institutions in the country, many of them originally of views on the subject opposed to his own. Yet in all the records so made the results were

invariable,

uniformly in accord.

The weight of the statistical evidence given in the writer's book on the subject may be judged by some examples.

For instance, in regard to the first statement, showing that in mixed communities rice-eaters only suffer, others being exempt. This was proved by records of epidemics all over the world.

In the Malay Peninsula in particular, in a given year, 1901. statistics carefully collected showed, that of 45,022 *rice-eaters* treated in various Government Hospitals, no less than 8,159 or nearly *20 per cent. had beri-beri.* But of 3,566 admissions of races customarily not rice-but *flour-eaters*, only 16 had beri-beri, or *less than ½ per cent.* The exceptions making up this fraction were Sikh or Bengali paupers, some of whom were proved, and the others may reasonably be supposed to have been reduced to eating rice instead of their national diet of flour. Another, larger series of patients showed when analysed

83,719 eaters of uncured rice, of whom 16,325 or again 20 per cent. had beri-beri.

With these were treated *6,903 of the non-rice-eating races, of whom again one half per cent only had beri-beri,* this fraction including as before individuals who in every *investigated* instance proved to have been subsisting on rice instead of their customary flour.

In the last three decades no less than 1,500,000 rice-eaters have been in-patients in the various Government institutions, of whom 300,000 had beri-beri; and ***100,000 natives certainly not rice-eaters, of whom NONE had beri-beri.***

As regards the differences among the rice-eaters, one of the tables given in my book showed among

Tamils,

customarily eaters only of cured rice, 45,135 admissions, of whom less than ½ per cent had beri-beri, the fractional exceptions (which "prove" the rule) including all those Tamils who for one reason or another had given up their cured for other sorts. Uncured rice-eaters admitted with these were the 83,719 named above, of whom 16,325, or 20 per cent. had beri-beri.

Of the 1,500,000 rice-eaters treated in the hospitals, at least 500,000 were Tamils. *No authenticated case of a Tamil known to be subsisting only on cured rice was recorded in all this vast series ;* nor has one indeed been since discovered.

The use of "*fresh*" rice is almost entirely confined to

Malays.

The fact is well established (and may be confirmed by whoever chooses to enquire) that natives of this race living in their own Kampongs, and subsisting only on rice of this kind

never get beri-beri.

But in the prisons, the barracks, the towns, on mines, estates, on ships, on journeys, in short wherever he has to use uncured shop rice, the Malay is peculiarly apt to get beri-beri. Accordingly in a series of 4,748 admissions of Malays to hospital, a proportion of 3 per cent was for beri-beri incurred under circumstances such as described.

The vast majority, or to be exact, 97½ per cent, of all the cases of beri-beri was furnished by the

Chinese,

all users of uncured rice. Figures compiled by the writer showed that between 1881 to 1892 there were 466,693 admissions of Chinese to 32 hospitals which had accurate records. Of these 123,639 had beri-beri, and

19,459 died

of it in the hospitals ! All this in a population averaging under 500,000 !

The evidence for the truth of the contention made, it will be seen, was enormous. It may be accepted as demonstrated—as having been then demonstrated—for the first time and completely by the present writer's work,—that the cause of beri-beri is the consumption of uncured, or as others call it, "white" or "scoured" or "polished" rice. It is a conclusion indeed which all but the wilfully blind must see. It stares out of the facts, naked, adamantine, unassailable,—a proposition, a discovery as completely proved, as securely founded as any ever before brought forward in medicine.

More important even than the discovery of the cause of the disease, was

the recognition of its remedy.

It might have been irremediable!

But it became obvious that if in a country, throughout every corner of which beri-beri was rife, the only class of native that was absolutely exempt from its ravages was the cured-rice-eating Tamil, himself in every other respect far more sickly than any other race, then the adoption of cured rice by other natives should secure to them equal immunity, its adoption in Government Institutions should mean the absolute prevention of beri-beri in those Institutions.

This was the remedy, the simple, inexpensive, but completely efficient remedy, placed by the writer in the Government's hands, and

used by them

(with a success as to which I shall presently give some details) before—this is a point to emphasise—any worker at the Institute had contributed a single iota to the issue.

THE ATTACK upon the camp of the infectionists was vigorously but not critically opposed, for their defences were weak, and their retreat became a rout, which has lately been made complete.

My conclusions, first put forward in a paper, read at a Congress in 1901, were received by my colleagues with polite but uniform incredulity. My friend

Dr. Travers

opposed them with an account (in 1901) of an experiment which he had made at the two Selangor Gaols *in 1895*, which he claimed completely disproved all possibility of beri-beri being dependent in any way upon food.

Sir Patrick Manson

hailed this observation as "completely refuting" the rice-theory, declaring at a meeting of the British Medical Association at Oxford in 1902, that it "proved up to the hilt" that between food and beri-beri, rice and beri-beri, there was *no connection whatever!*

My friend,

Dr. W. Gilmore Ellis,

the present accomplished Principal Medical Officer, S. S. in his official report to Government on the Asylum for 1902, wrote:—"as to the cause of the disease [beri-beri] I regret being unable to report any progress. I am convinced and have been for many years that the consumption of mouldy microbic or otherwise diseased rice is *not* the cause." And he went on to narrate an experiment made by himself some *13 years before*, which he claimed completely disproved any connection between beri-beri and food.

Writing in the British Medical Journal of November 14th 1903, Dr. Ellis repeated this statement, and gave an account of another observation "entirely" as he thought "putting Siam rice out of the question as a cause of beri-beri."

It soon appeared that there was an unobserved source of error in Dr. Travers' observation, which entirely vitiated his conclusions.

And Dr. Ellis, after long coquetting with the rice-theory, has since announced his complete conversion—although I have not had the gratification of learning that he attributes any share in the production of this happy result to the evidence adduced by me!

Sir Patrick Manson, to whom my larger work was submitted in manuscript in 1904 before publication, whose attitude against rice had been so emphatic, was as naturally might be expected, not easy to convince. But he recognised at once the formidable nature of the new arguments, and it was to his recommendation that I owed the opportunity afforded me later by the local Government (at the suggestion of the Colonial Office) of conducting

an experiment specially designed

to test the truth (or untruth) of my theory in a manner which would afford demonstration even to the dull.

Sir Patrick's expectation was, that the experiment would overthrow my views, and although the event was on the contrary to confirm them, I have not yet heard that Sir Patrick has recanted his own.

Another redoubtable opponent of the rice-theory was

Dr. Durham

who sent out on a Commission (for which was paid a thousand pounds) to investigate the disorder on Christmas Island, published in January 1904 conclusions absolutely opposed to food theories in general and the rice-theory in particular.

It is evidently not given to all to understand evidence!

Among those who, even after reading my work, required "yet a sign," was

Dr. William Fletcher,

who was in charge of the Selangor Lunatic Asylum, an Institution as we have seen little better than a beri-beri death trap.

Dr. Fletcher decided to try the matter for himself by direct experiment in the Asylum. He stated, in the published account of his results, that at the commencement of the experiment, he held the opinion "that rice was neither directly nor indirectly the cause of beri-beri. His experiment consisted in placing half the inmates on the best rice of a par-boiled variety which was obtainable, the other half on good Siamese rice. No other change of any kind was made in the conditions of the patients, who mixed together freely by day and used alternately the same dormitories.

The experiment lasted from December 5th, 1905, to June 1908. The result was that

in the uncured rice-party, in 1906, 115 per cent. were attacked

(38 cases in a daily average population of 33—the population is of course a changing one); *in 1907, the attack rate on the uncured-rice-eaters was 77 per cent*; in 1908, (six months only) it was 19 per cent.

Among 120 patients on uncured rice there were 41 cases, and 18 deaths from beri-beri.

Among the equal party

on cured rice

there arose throughout the 2½ years

not a single case

and there were no deaths.

"*Contrary to expectation*, the *result of the experiment as far as it goes*," says Dr. Fletcher, "*Is to prove the truth of Dr. Braddon's contention that uncured rice is the cause of beri-beri.*"

This observation of Dr. Fletcher's, with its clear and unambiguous result, was the sole positive addition made (outside the writer's researches) to our knowledge of the cause of beri-beri up to that time. Although itself wholly unnecessary, a mere drop added to the ocean of evidence already presented by me, Dr. Fletcher's observation had at least the merit of convincing himself, and thereby relieving the unhappy inmates of his

Asylum, who were thenceforth dieted on cured rice only, with the result that from that day to this

no more cases

of beri-beri have appeared among them.

We come now to the part played to

the Institute of Medical Research

(or as it is now called the Pathological Institute) in the elucidation of the disorder.

The Institute was originally founded on the recommendation of a Congress of Medical Officers in 1897. For a long time a brass tablet in the entrance hall of the building bore the legend that it was "suggested" by Sir Frank Swettenham and erected under the 'direction' of Dr. Hamilton Wright—whence it may be inferred that all the brass was not used up in the tablet. The chief object of Government seems to have been to provide an establishment in which highly-paid experts might be enable to devote their whole time to the investigation of the diseases of the country, assisted by all the resources which Government could place at their disposal.

The

first Director

of the Institute, DR. HAMILTON WRIGHT, after spending a year or more in proving the existence of Malaria in the Native States (a discovery which however had been anticipated) proceeded to investigate the question of beri-beri. Dr. Hamilton Wright published four extensive monographs on the subject. His principal conclusion was that the existing professional notions about beri-beri were a complete muddle, which he fortunately was able to set right! As the result of a prolonged experimental investigation into the disease at Pudu Gaol 1901-1902, *during which all the prisoners were fed on uncured rice*, he announced that the rice could not in any way be considered to be the cause of the disorder *because it had been boiled* before it was eaten! Any opinion to the contrary Dr. Hamilton Wright derided, as that of a

"bold and badly informed theoriser."

The next Director of the Institute,

Dr. C. W. Daniels,

also published a work on beri-beri, in 1906. In this work, after quoting at length most of the evidence provided by the present writer as proving the orgin of the disease from uncured rice,—proofs, the cogency of which the reader has already realised—Dr. Daniels asserted that "*the hypothesis that diet, or any article of diet sound or unsound can originate the disease has in my opinion* **no facts** to support it"!

(My italics.)

The establishment of the rice theory—almost universally accepted as it is by scientific observers in the East to-day—owes, then, nothing to these two observers; and it is clearly not to their work that His Excellency the Governor of the Straits Settlements can have referred when he sought to attribute the present proved possibility of eradicating beri-beri—the discovery of its cause, and the means of preventing it—to work done at the Institute.

The successor of these experts at the Institute was the present Director,

Dr. H. Fraser,

whose contributions to the subject will next be considered.

I have mentioned that the Government had consented to grant me an opportunity to demonstrate by direct experiment the truth of the views as to the cause of beri-beri which, in season and out of season, both in printed and published, and written official communications, I had ever since 1901 urged upon them.

The Official Medical Adviser of the Resident-General was (by virtue of his office!) the Director of the Institute of Medical Research. We have seen how both the first occupants of this post had failed to understand the evidence by which the origin of beri-beri was indeed already completely proved before they came upon the scene. It is not surprising therefore that their successor Dr. Fraser should have proved equally unillumined, and should have advised Government that my views could not be accepted until demonstrated by further experiment, to be made preferably by himself, or at least under his own control.

After much search the conditions necessary for a suitable observation were found in Jelebu, at

Durian Tipus.

Here my friend

Mr. T. R. Hubback,

of big-game-shooting fame, was engaged in making a road through the wilderness, on which three or four hundred Javanese labourers were employed. The interference with work entailed by daily medical inspection of coolies, for the purposes of an experiment, means loss of time and money, and will not willingly be allowed by many employers merely for the sake of science, or humanity. But Mr. Hubback already knew and had benefited by the application of my views about beri-beri, an epidemic which had appeared among his labourers formerly, having been arrested by the use of my remedy—cured rice. Both as my friend, and scientifically, he was interested in seeing the official test of my views made successful. With great generosity and public spirit he placed the whole of his labour force at my disposal for the experiment, and became the Mæcenas of the enquiry.

I received the official permission of Government

to conduct the enquiry

early in 1907. It was intimated that Dr. Fraser, as Director of the Institute and representing the Government, would be *associated* with me to check and report on the results of the enquiry, the conditions of which were left to us jointly to arrange.

The experiment was designed to ascertain whether in a body of labourers kept free from chances of outside infection, beri-beri would occur in those using uncured rice, at a place and time when a similar number of the same labourers, equally circumstanced in all other respects except that their diet was to be of cured rice, should remain exempt from the disorder. Supposing that this happened, supposing that all the circumstances had been made equal for two suitably large parties (except for the difference in rice) then if beri-beri occurred, and if on its occurrence it attacked exclusively the uncured rice-eaters, it was to be held that the rice-theory would be

officially confirmed.

Well, the experiment was made. To assist Dr. Fraser, and in order that everything might be thoroughly controlled, Dr. A. T. Stanton was appointed as his assistant, to reside at the scene of operations, 60 miles beyond Seremban.

The event, into the details of which I need not now enter, was to completely confirm my theory. All chances of infection were ruled out. The conditions as to food, labour, housing, clothing were alike for both lots of coolies. But at every station wherever a gang of men was *on uncured rice* (and first and last no less than six stations were occupied by them)

beri-beri broke out.

On the other hand, among the cured rice-eaters, whether they occupied the same stations before, after, or simultaneously with the others,

no case

of beri-beri at any time occurred.

The work of the investigation was conducted *jointly* by Dr. Fraser, Dr. Stanton and myself—and it is fair to add that by far the greater part of it, all the arduous labour of keeping the records, as well as the constant medical supervision of the coolies was the share of Dr. Stanton, and was admirably done by him. The experiment was officially

my experiment.

It was the opportunity granted me by the local Government (on the recommendation of the Colonial Office) to prove the truth of the views of which I had been the first, and then still was

the only exponent,

the demonstration of which was held, and rightly held by Government (at that time at least) to be of the greatest importance to the country. Not only was it thus my experiment *officially*, but the means, the material, the opportunity was—through Mr. Hubback's generosity to me personally—of my providing. The actual observations, the noting of the results obtained, was as I have said, made jointly by the three observers.

Now it will hardly be credited, but is none the less true, that in no less than *five successive communications* made by them to the Government, and the Medical Press, dealing with the enquiry, and its resultant proof of the correctness of the rice-theory of the beri-beri, Drs. Fraser and Stanton put forward the actual observations,

appropriated the results

gained, *as entirely their own* !

Nowhere in the text of any one of these papers is the present writer (whose the investigation really was) anywhere referred to as having either initiated, or organised, or contributed to the research !

There is plagiarism in literature, there is piracy in music (and on the high seas), there is poaching on game preserves, and pilfering in every walk of life—but what is to be said of the brasen appropriation of other workers' results by your scientific egoists,

pirates of research ?

Their *share*—Dr. Fraser and Stanton's *share* in the above investigation—the result of which was, after all, but to bring one brick more to an edifice already built—forms

the sole contribution

which has so far been made to our knowledge of the cause of human beri-beri by workers at the Pathological Institute,—those workers to whom H. E. the Governor of the S. S. has chosen to attribute the merit of having at last made possible the prevention of the disease !

THE CAUSE of beri-beri, then, is the consumption of uncured, "scoured" or "white" rice. That, in this country, is the sole effective cause of a disease which, as we have shown,

yearly kills thousands

of the young and able-bodied.

It may be

prevented absolutely

by the use of rice prepared by a process already in commercial use—the parboiling process.

These facts, unknown, or at least unrealized, before the writer pointed them out, form a definite and practical, an economic as well as scientific discovery, which it is now surely the duty of the Government

to apply

for the benefit of the population at large.

All that is necessary is for them to discourage (if they cannot prevent) the importation and use of rice of the kind which has been proved to be noxious: to make the sale of such rice if not illegal, at least unprofitable.

It will be no hardship for the rice mills to turn out rice which will be harmless, for this will actually save them labour, in the omission of the "scouring" of the grain, which removes from it the essential nutrient portions, the preservation of which in parboiled rice constitutes the sole difference whereby the latter remains fit for human food.

A tax

of a dollar or two on every bag of such rice imported would effectually restrict its use among those who now consume and suffer from it:— and would incidentally bring in much needed grist to the mills of the local exchequer of the Straits Settlements.

Of the actual working efficiency of the remedy made known by the writer in the prevention of beri-beri in Public Institutions, (namely, the substitution of cured for uncured rice in the diets) the Governor is well aware. My views and recommendations were placed in His Excellency's hands in November 1904. The adoption of cured rice in all the Public Institutions of the Colony was made

by His Excellency's order

immediately after that date.

The results were as immediate and gratifying as they were extraordinary.

In the Singapore Prison, as we have seen, this simple change brought about freedom from the disorder for the first time since 1898.

In the Lunatic Asylum, according to Dr. Ellis (see British Medical Journal, October 1909,) the same result was secured. That pest-hole of beri-beri became freed of it

for the first time in its history

only when cured rice was wholly substituted for the uncured. We have seen the same result in the Selangor Lunatic Asylum.

Not only was the disease thus stamped out of Institutions in which it had long been practically permanent, but

in the hospitals

the mortality among cases *admitted for beri-beri* fell in marvellous degree, everywhere, immediately on the substitution of cured for the uncured grain. Thus in the Tan Tock Seng Hospital, Singapore, where cured rice was introduced in 1905,

the mortality fell at once from 48 to 18 per cent.

In Province Wellesley there was reduction from 44 to *15 per cent*: at the Malacca Hospital from 28 to 7½ per cent: at Jasin from 41 to 9 per cent, and so on.

At Christmas Island, where the Medical Officer had acted on my advice earlier, it was reported that the result was "most marvellous and immediate"—instead of *95 deaths in ten months*, there were only *12 in the next fourteen*.

In the Native States (owing to the obstinacy of my colleagues!) cured rice diet was only adopted, (and then at the instance of Government) much later: but here too, similar results were gained.

At Batu Gajah,

for instance, the death rate fell from *50 per cent* in 1907 to *11 per cent* in 1908: at Kampar, it was reduced from 37 to 9½ per cent—and so on.

As some 10,000 cases are treated annually in all the hospitals of the Colony and Federated Malay States, the reduction of the death rate from the

frightful figures

formerly prevailing means an enormous saving of life. If only 10 per cent die now where 30 or 40 per cent died before, the number of

lives saved

is two or three thousands *annually*.

Of this achievement, this one fruit of his labours, no one has (so far) sought to deprive the writer.

* * * * *

THERE is another side to the beri-beri question, of great scientific interest. What exactly is the difference between the rice which produces beri-beri and the rice which does not? In what way does that difference operate to produce the disease?

If you swallow something, and the result of swallowing that something is that you become diseased, the matter you have taken may rightly be described as poisonous. It will not alter the correctness of the description to know that if you take something else—an *antidote*—with the poison, it will render the latter inactive. Now uncured rice, *used in the only way in which it ever is used* by the native, namely, as a staple food, produces beri-beri. The ignorant public therefore ought to be protected against its use, as against that of any other poisonous commodity —but that is another story.

On the academic question, whether beri-beri results in the uncured rice-eater because he has taken something *more* than is wholesome, or *less* than is wholesome, there is division among the scientists. The writer's view is that uncured rice is poisonous

in itself;

a position not contradicted by the fact that to restore to such rice the part removed artificially (the bran, etc., which in cured rice is retained) will antagonise or prevent the poisonous action. A simple proof of this is, that if you deprive a fowl (which easily gets beri-beri) of everything except air and water, it dies certainly, but slowly, after perhaps twenty days or more, of starvation—*no paralysis* is produced. But if in addition to the air and water, you give a fowl *uncured rice*, it will die much more rapidly, and with all the paralytic symptoms of *acute beri-beri*.

It is in this field, of the chemical differences between the poisonous and non-poisonous rices, that the workers of the Institute have added

a little

to our knowledge—in confirmation of facts for the most part already well ascertained.

Thus the chemist of the Institute, Mr. R. J. Eaton, made determinations of the compositions of various foodstuffs and rices in local use. He also specially determined for Dr. Fraser the phosphorus content of the rices, finding it more plentiful in fresh than in uncured, and in cured rice than either.

Dr. Fraser confirmed (though he barely acknowledged) an observation, long previously made, and subsequently (though he seems not to have been aware of this) greatly extended by Eijkman, showing that fowls fed on white (uncured) rice get a form of paralysis like beri-beri, which is prevented by restoring to such rice the bran, etc., previously taken from it in milling.

Observing that the capacity of rices to produce this beri-beri of fowls varied inversely with their content of phosphorus, Dr. Fraser was led to associate the deficiency of the element with the causation of the disease. This idea again (although he seems not to have known it) had already been anticipated by others, and

disproved.

Beri-beri is not a "phosporus starvation."

A single contribution to

the practical side—

the prevention of beri-beri—was made by Dr. Fraser.

As a remedy against beri-beri, alternative, or to be preferred to the simple course suggested by the writer (which is to avoid wholly the use of uncured or spoiled rice, substituting for it always the cured sort, which being already on the market is easily obtained) Dr. Fraser would have users of white rice buy and keep beside them a little of

the "polishings,"

to be added separately in due quantum to the daily meal!

These "polishings" consist of the bran and fine offals (sharps) removed from rice in the milling process of "scouring" (not "polishing") which renders it white. Mixed with the grit of the millstones, the dirt of the machinery, and the floor-sweepings, the "polishings" are sold to natives and used by them as cattle food ("dedek.")

The exact amount of "polishings" to be added to each meal by the consumer is not indicated. But in Mines and places where the proposal was put into practice, no doubt the cooks and kepalas would be enabled easily to ascertain this, from an analytical table (to be furnished by the Institute of Medical Research) which would be

hung up in the Kongsis

for reference.

The simple hen, uneclectic in its dietetic ways, accepts the "polishings" no doubt readily enough. But imagine the Chinese coolie, already exacting enough, asked to supplement his rice with "*dedek*." The high phosphorus-content of it would never appeal to him ! A question the practical mind, pondering on this quaint proposal of Dr. Fraser's, is moved to ask, is :—If the "polishings" are so essential to the diet, that they must be restored again to white rice whenever this is eaten, why allow them to be removed at all ? Why indeed ? But it was incumbent on the Institute of Research to contribute something

something practical

to a practical issue—if possible not the same as anything proposed before—and this is it—a suggestion which could not have been bettered by the Wise Men of Gotham.

But perhaps we are taking Dr. Fraser too seriously. He is nothing if not humorous and in this matter of the "po-lishings" he may be only poking fun at us—a pawky

LITTLE JOKE ?

THERE is one more side of the beri-beri question—the dollar side.

The 150,000 young labourers who have died of beri-beri in the 30 years of the past represent, at their usual cost of importation per head, a direct loss of about

nine millions of dollars.

The 10,000 cases of beri-beri treated *annually* in our hospitals (each on an average for a month) cost Government *annually* $100,000. The loss of the labour of these patients before they reach hospital, and of the many more who never reach hospital at all, costs the public, it may be estimated, far more. Not less than

a quarter of a million dollars,

probably, represents

the yearly cost

to the community of this one disease.

All this loss will go on recurring year after year, until Government adopt the one efficient remedy, which is simple and practical—and may even be made profitable—of prohibiting absolutely the sale of spoilt rice as food. *Spoilt rice*, in the most exact sense of the word, these uncured commercial white rices are rendered through the deprivation of their essential nutrient portions in milling worse than useless as food, a not merely deleterious, but definitely

dangerous article.

Not long since the Government engaged at considerable expense the services of a Sanitarian of great experience to report on the causes of the scandalously high death rate of the Colony (40 per mille) and to suggest remedies.

Professor Simpson

made many suggestions, one and all requiring great sums of money to carry out. He was unaware that the death rate could be reduced, almost at a stroke, by nearly a quarter, by any means so simple as that by which, I have shown, beri-beri may be not only exterminated but even made to pay for its own extinction.

The great (like the Syrian of old) are often averse, as we know from counsels of simplicity. But here obviously there is lying at hand a great sanitary reform, which it is the instant

duty of Government

(or if they will not, then of the community) to have carried out.

I HAVE perhaps now made evident something of the significance of the beri-beri question, of the importance to the country of the discovery which has been made (after so many centuries) of its cause, and the means of preventing it.

As a public service that discovery has

a value—

the exact measure of which is the enormous annual losses which may now, by its application, be prevented. It is surely fitting that those who have rendered this service should receive the recognition of their achievement : and equally as unfitting that the Government, representing the public, should bestow that recognition where it is not due.

It is always invidious to be the advocate of one's own claims, but it is not part even of the scientist's duty to stand idle while the fruits of his labours are appropriated by, or even on behalf of others : and by the consent of silence to acquiesce in his own effacement.

I do not claim, I trust that I have nowhere implied, that I am the first or the only medical observer who ever attributed to rice the causation of beri-beri. There is nothing new under the sun—and certain—not many—others have in other countries been led before me to the same conclusion, which some—notably Van Dieren—have supported with very striking evidence. The labours of all such of my predecessors in the field have, so far as I have been able by diligence to make myself acquainted with them, been duly recorded in my work.

But I do claim that in this part of the world, in the Straits Settlements and Federated Malay States, among British Investigators I stood first and

alone

for the now accepted theory, and maintained it with evidence,—maintained it moreover against the opposition of all my colleagues, and in particular of the reputed experts on the subject, and the official advisers of Government. I claim that in the evidence, the *facts* laid by me before the Colonial Office in 1904, and published later,—the truth of which has never been impugned—

proofs were given of the origin of beri-beri from rice, for the first time, which were complete and incontrovertible.

Nor have they since in any essential been controverted.

I thus claim to have *demonstrated* what had previously only been *surmised*, and nothing which has been effected since has done more than add a confirmation to my theory.

I may assert (without, I think, any fear of contradiction) that the remedy for beri-beri (which so naturally flowed from the observation of the cause) which was suggested by me, was *first* suggested by me,—was moreover,

the first efficient means ever suggested by anybody for the prevention of the disease.

That remedy was placed by me in the hands of Government, and

was utilised by them,

before any communication by any other observer had been made to them, even confirmatory of my theory.

The result

of its application was (as has been seen) to bring about the immediate and complete cessation of the disease, for the first time in their history, in the Gaols and Asylums in which it was used. By it, moreover, the mortality of cases of beri-beri, against which nothing had ever previously availed, was brought down from appallingly high to very low figures, and the saving of several thousands of lives effected annually.

To the achievement of these results the workers of the Institute of Research, after a long period of active and ill-reasoned opposition, contributed, towards the end,—

what ?

A *share* in one solitary (confirmatory) observation—an observation of which they nevertheless thought so well as to claim the whole.

Yet it is to work done at the Institute that H. E. the Governor of the S. S., would alone attribute the credit of the conquest of beri-beri. !

Surely it is not too much to ask H. E. the Governor of the S. S., now placed in possession of *the facts*, to correct an attribution so unjust, and to manifest his appreciation of a public service by public recognition of its real author.

W. LEONARD BRADDON.
M.B.,B.S., LOND., F.R.C.S., ENG.

SEREMBAN,
January 20th, 1911.

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A GENERAL ACCOUNT OF BERI BERI

AS SEEN IN SYDNEY,

BASED ON ORIGINAL OBSERVATION.

BY

CYRIL ERNEST CORLETTE, M.B., Ch.M., Syd.,

Senior Resident Medical Officer
Sydney Hospital.

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A GENERAL ACCOUNT OF BERI BERI

AS SEEN IN SYDNEY,

BASED ON ORIGINAL OBSERVATION.

DURING the last few years an apparently new disease has come very prominently into notice in this and other Australian colonies. The commonest symptoms complained of have been pain and tenderness of the calves, and weakness or "tiredness" of the legs, usually accompanied by œdema in lower part of legs, especially in front of tibiæ, and pain in the front of the chest. So far as my experience goes, the disease has been entirely confined to the Chinese. Three cases, one fatal, however, I have seen in Japanese. Though attention has only been attracted to the disease during the last three or four years, in which it has become markedly more prevalent and more severe, cases appear to have occurred here and there for many years. The Rev. Soo Hoo Ten, of Sydney, tells me that he saw cases at least fifteen years' ago, and a few now and then ever since. I have made extensive enquiries among the Chinese and they all, without exception, say that though the disease has been known for a long time, it has become common and severe only within the last five years.

The Chinese among whom I have made enquiries have been mostly from Canton and its district. They do not seem to have been acquainted with a similar disease in their own country, though their observation and memory cannot be taken as very reliable evidence on this point.

There is strong reason to believe that this disease was well established in Sydney long before its true nature was suspected and recognised, for reference to past hospital records show a considerable number of Chinese patients returned as "locomotor ataxia," "rheumatism," &c., which cannot reasonably be doubted to have been really cases of the disease under discussion, and reference to the notes of the cases confirms this opinion. In this connection, as throughout, it must be borne in mind that these patients do not speak English, and there is in consequence considerable difficulty in getting a history or a proper account of the symptoms, and even the friends who may endeavour to interpret often speak very little better English than the patient.

The patients have often been many years resident in Australia.

The same insufficient appreciation of its nature must also have existed outside the hospitals, and indeed I know that such was the case. It is scarcely more than three years' since the tenderness and weakness of the legs so often met with was (generally) recognised to be really due to a peripheral neuritis, and it is only within the last twelve months that this peripheral neuritis has been accepted as really due to Beri Beri, which must now be placed among the list of diseases known to be endemic in Sydney. I began the systematic study of the disease early in 1892 and became convinced that it could only be Beri Beri in a mild form, and further observation has only served to confirm my original opinion. Dr. Molloy, of the Melbourne Hospital, was one of the first to publish his suspicions of similar cases seen in Melbourne in a paper read at the Intercolonial Medical Congress in September, 1892, in which he describes cases of peripheral neuritis among the Chinese of Melbourne. Dr. James Graham, of Sydney, read a paper on Peripheral Neuritis at a meeting of the Medical Section of the Royal Society in Sydney in July, 1893, in which he describes a form as existing among the Chinese of Sydney which he at that time did not consider as due to Beri Beri. His account of the symptoms differs in some respects from those observed at the Sydney Hospital.

Dr. R. T. Paton, of Sydney, who has seen the disease in the East, has come to the conclusion that it is the same as that existing in Sydney, and stated his opinion in a paper recently read at a meeting of the New South Wales Branch of the British Medical Association.

The disease is usually a chronic one, presenting all phases of severity, from a simple feeling of fatigue in the legs, with some tenderness of the calves, scarcely sufficient to compel cessation from work, to general and helpless paralysis.

But there is another form, with very acute symptoms and rapidly fatal termination, with distinctly characteristic and easily recognisable clinical features. This form may supervene in cases which have begun like others which pursue a chronic course throughout, the severe symptoms coming on quickly and carrying off the patient sometimes within 24 hours.

It is not unusual for a man to have had several relapses of the disease, with intervals of freedom. One patient had had the disease seven years before, three years before, and one year before, and was in hospital with his fourth attack. Another was said to have been three times in hospital; he had had the same disease two years before.

On account of imperfections in diagnosis it is impossible to get a correct record of the number of cases admitted to the Sydney Hospital in years previous to 1892. In 1892 there were 5, and probably more, admitted, in 1893 there were 23, and in 1894 there were 29, or 27 if we exclude two Japanese admitted from a vessel in the harbour.

Of the 52 consecutive cases thus admitted, 5 were admitted in January, 1 in February, 6 in March, 3 in April, 8 in May, 3 in June, 5 in July, 3 in August, 5 in September, 7 in October, 3 in November, 3 in December. The two Japanese were admitted in October. It will be seen that there is a slight preponderance of cases in the months March, April, and May. There were about two fatal cases in 1893, one being from a steamer in the port. There were 6, perhaps 7, fatal cases in 1894. Two of these were Japanese from a steamer trading to the Straits Settlements, China, and Japan, &c.

ÆTIOLOGY.

A great variety of theories have been put forward as to the causation of the disease. The most generally favoured has been that ascribing it largely or wholly to dietetic causes, especially to a fish diet. Others have thought that the habitual consumption of opium had something to do with it; others again have looked to insanitary conditions of the dwellings and overcrowding as a likely agent. The question is not yet fully solved, but there are very strong arguments in favour of the theory that the essential cause is special miasm or infection of some kind, inhabiting the places where the disease is rampant, but requiring considerable and extended exposure to its influence in order to produce the disease.

The question of diet I have studied in nearly every case. The patients have in the large majority of cases lived well, and had plenty of food. The flesh diet has been chiefly pork, fish, fowl, and ordinary butchers' meat. Pork, fish, and fowl are always mentioned as favourite articles of diet. Rice is the main st ~~the [illegible] in the city, [illegible]~~, ordinary garden vegetables are largely used. Bread is not used to a very large extent. Tea is the favourite beverage. Spirits are not taken at all by a fair proportion, but a few take a daily allowance either of brandy or what they call "Chinese spirit." As a rule, however, spirits are only taken as an occasional luxury, and on special occasions. In no single case have I been able to find a patient who has undoubtedly been accustomed to take spirits to excess. Beer is never taken, wine very occasionally. The abstemious and sober habits of the Chinese in this respect are a matter of common knowledge.

Thus alcohol, a well-known and common cause of peripheral neuritis among Europeans, cannot be credited as a casual agent in the variety under discussion.

Some have expressed the opionion that the consumption of opium is a probable factor in the causation of this disease. The practice of taking opium, either in the form of pills, or by the method of smoking, is common and widely diffused among the Chinese in Australia, but I am unable to find any valid reason for suspecting that this has any direct causal influence in this disease. In the cases I have investigated, there has been a large proportion in which the opium habit was certainly not present, in others the presence of the habit was doubtful, and in others the habit was acknowledged. In many at least of these the practice was carried on in moderation. So far as I am aware, the opium habit in other races has not been known as a cause of any kind of peripheral neuritis. It is, however, quite possible that the habit, when carried to excess, may, by lowering the general health, act as an indirect agent, by helping to lower the resistance of the body to other more direct causes. The same would apply to anything else prejudicial to the general health.

Lead-poisoning is known as a common cause of peripheral neuritis, both of the parenchymatous and interstitial variety. The disease under consideration presents clinical characteristics quite distinct from those found in lead-poisoning, as will become apparent upon examination of the symptoms. Apart from this, no history could in any case be obtained which would justify a suspicion of lead as a cause. Arsenic can be similarly eliminated.

Occupation seems to have little or no influence. The disease is found indifferently in hawkers, shop assistants, carpenters, and gardeners.

It is impossible to form a proper estimate of the influence of age from the fact that the Chinese are only sojourners in the colony, coming here at any time after they have reached years of discretion, and leaving after they have saved a certain amount of money. In 50 cases, there were none under 20, 5 were 25 years and under, 9 from this to 30, 12 from 30 to 35, 8 from 35 to 40, 11 from 40 to 45, 2 from 45 to 50, and 2 from 50 to 55.

The question of the influence of sex is also at present to be left open, because the Chinese population consists, with scarcely an exception, of males. A certain number of European women inhabit the Chinese quarter, but no case from among the women has yet found its way to the Sydney Hospital.

An important ætiological consideration arises upon investigating the localities in which cases have occurred. It is found that the disease seems to exhibit a very marked preference for certain houses, or groups of houses. There is no doubt that where one case occurs in a house there is an increased probability that other cases co-exist, or will arise. I have met with very numerous examples showing this peculiarity of the disease. I may quote as an example one street in Sydney in which I made careful enquiries on the spot from a number of the inhabitants. In this street every house, with the possible exception of one, had furnished cases of the disease, some more, some less. In one house I gathered particulars of what seems to have been a fatal case, which presented the usual symptoms, and by the friends was regarded as the same disease as that prevalent among the others. Several very intelligent men assured me of their belief in the identity of the disease, and, from their account, I have very little doubt that the diagnosis was correct. From another house, in another street, came two patients in the one day, following one admitted shortly before. From a cabinet-making establishment in another quarter, as recorded by Dr. Paton, nine cases arose. One of these was a patient in the Sydney Hospital for nearly three months, suffering from severe symptoms, and very advanced paralysis, including the muscles of the neck and face, which showed altered electrical reactions. After improving in the Sydney Hospital he went out, able to walk, but in a little over two months he was seized with symptoms of the acute, fulminating form, was admitted to the Coast Hospital, and died of the disease next day.

At another place, whence a rapidly fatal case came to the Sydney Hospital, there had been four previous cases of the disease. Dr. Molloy, in his paper, draws attention to an instance in which nine cases came from one establishment.

The partiality of the disease for certain localities exists independently of the drainage or character of the soil, the greatest possible variety being found in these conditions. The disease appears to flourish equally well in low, swampy places as on the side of a steep and rocky hill, with good drainage.

I am not able to speak of the relative prevalence of the disease in the country as compared with the town, but it seems to be as bad in distant suburban houses as in the heart of the city.

The *Anchylostoma duodenale*, a worm which has by some been supposed to cause the symptoms of Beri Beri is, I believe, not known in Sydney.

SYMPTOMS.

The first symptoms described are a sensation of what is universally described as "tiredness" in the legs. At the same time, or a week or two after, the patient gives a history that the legs began to swell, and he often adds that they pitted on pressure. The "tiredness" and swelling are at first noticed after exertion, but soon it becomes more constant, is noticed whenever he stands, and the "tiredness" becomes transformed into real pain, sometimes severe, and incessant, with exacerbations. Together with the increase in the "tired" feeling the patient feels a sensation of weakness in the legs, and an alteration in gait is noticed. The weakness frequently goes on to such a degree that the legs will not support him, and he has to take to bed.

As the symptoms develope in the legs, the hands and forearms become gradually affected in like manner, but the symptoms are later in time, and less marked. The first thing the patient notices is an inability to perform the finer and more complicated actions properly, the fingers becoming less dexterous. This seems to be in part due to a sensation of numbness. About the same time, the hand is found to be distinctly weak, and this goes on in some cases to such an extreme that the patient is unable to feed himself, or use the hands at all. The weakness being most marked in the extensors of the forearm, and the front of the leg, the "dropped wrist" and "dropped foot" position is assumed.

The muscles affected become at first flabby, and lose tone, and then waste coincidently with the progress of the weakness. The wasting is often extreme, and the atrophy of the muscles of the hand in the thenar and hypothenar regions and in the interossei is very conspicuous. In the mildest cases the muscles become flabby, but do not perceptibly waste.

Coincidently with the weakness, the muscles become extremely tender to manipulation, and the patient can sometimes hardly bear them to be touched. Beside the tenderness there is in many cases severe and continuous pain, making the patient's life one of constant and acute suffering. It is occasionally much worse on one side than on the other. It is most marked in the legs.

In the acute fulminating cases which I have seen, the pain and tenderness of the muscles was slight.

In the cases where the patient is able to walk, the gait becomes altered. On account of the weakness of the flexors of the foot the toes are not sufficiently raised, and the knee is therefore lifted higher in order to enable them to clear the ground. In a still greater degree of weakness, progression is slow and difficult and the feet are never completely lifted from the ground but dragged along it.

The tenderness of the feet and of the muscles of the legs has also a modifying influence on the gait. I have not noticed ataxic symptoms. The patients can continue to stand when the feet are placed close together and the eyes shut.

The electrical reactions of the muscles undergo marked alterations in this disease. The normal reaction to galvanism is changed, so that ACC becomes equal to, or greater than, KCC. The reaction to faradism is frequently lessened, and in some cases practically abolished. I have tested the reactions as a routine practice in a great number of cases and have never failed to find an alteration in galvanic irritability. I have in most cases gauged the current by the number of cells involved, but I have recorded some in milliamperes. The relative irritability of the muscles is difficult to estimate.

In the mild cases the legs only show the altered reaction, which is most marked in the extensors and peronei. Then the muscles of the thigh are affected, beginning with the quadriceps extensor and then showing itself in the muscles of the inner side and back of the thigh, and those of the gluteal region. The muscles of the hand and forearm, including the supinator longus, are affected as the weakness appears in the upper extremity. As the weakness and wasting increase, the altered reactions show themselves in the upper arm, the pectoral and scapular groups of muscles, the trapezius, sterno-mastoid, and the muscles of the face. Affection of the sterno-mastoid and trapezius has never before been recorded. I have found it twice.

The affection of the facial muscles is worthy of particular remark, as in alcoholic neuritis, which presents some outward resemblance to Beri Beri, the facial muscles always remain unaffected. Pekelharing and Winkler record affection of the facial muscles in five cases. I have found it in two.

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The electrical reactions in fulminating cases could not be taken, owing to the serious condition of the patient.

An alteration in sensibility of the legs and feet, and of the hands, is well marked in some cases. There is often a diminution in sensibility; sometimes there is a degree of hyperæsthesia, and numbness and a sensation of "pins and needles" is sometimes complained of. But on account of the meagre amount of English possessed by the patients and their friends who interpret, it is difficult to get a trustworthy account of their sensations. For example, in testing sensibility a patient will often say that he "does not feel" when he certainly does feel, but in sayin that he does not feel, or "no feel," he really means that he does not feel pain. It is often impossible to get over difficulties of this sort. The stock expressions of the Chinese patient are "too sore," meaning that he has pain; "too tired" and "too torpid," meaning weakness; and "no good," meaning a more advanced loss of power.

The plantar reflex is normal in the slighter cases, but becomes lessened and disappears as the weakness and wasting increase. Dr. Graham has stated that the knee-jerk is always lost, and Dr. Molloy states that the deep reflexes are "almost invariably" lost. This is certainly not corroborated by my own experience, which extends over nearly 60 cases. The constancy with which the knee-jerk is found present is very remarkable. It exists, in the large majority of cases still able to walk, often being obtained with the normal amount of facility. Even when the weakness is considerable, when great care is used, a slight knee-jerk can sometimes be elicited.

The light reflex of the pupil is normal. The accommodation reflex of the pupil has also been normal when tested, but this has not often been done owing to the difficulty in getting the patient to understand what he is wanted to do. The bowel and bladder reflexes have always been unaffected.

Patients suffering from this disease are very subject to attacks of sweating, most frequently confined to the head, face, and trunk, but sometimes general. The sweating occurs independently of external conditions of temperature, &c., and at any period of the day. The attacks are profuse and frequent in some patients; others are less affected. The body temperature remains normal during these attacks. I have been unable to find any previous record of this symptom.

Œdema of the legs probably occurs to a greater or less extent in every case. It is a very early symptom, coming on coincidently with the feeling of "tiredness" in the legs. It is increased by standing, or walking about. When slight in amount, it is only manifested by a little pitting on pressure over the lower part of the crest of the tibia. When more extensive, there is pitting on pressure over the parts about the ankle, and higher up the tibia. I have never seen a very great amount of œdema, and have never seen it higher than the knee. The face is often puffy in appearance, but there is no sign of pitting to be obtained, and no dropsy of the lower lids such as is seen in some cases of Bright's disease. The œdema usually disappears rapidly after admission to hospital for treatment.

I have almost constantly found two very acutely tender spots on the foot. One is on the dorsal aspect, over the first inter-metatarsal space, about an inch from the bifurcation of the first and second toes. The other is on the outer side of the foot, over the prominence of the cuboid. The first tender spot is over the internal branch of the anterior tibial nerve, where it bifurcates; the second spot is over the external saphenous nerve. These two tender spots I have not found in other cases of peripheral neuritis, but in Beri Beri the tenderness is often so severe that the patient cries out with the pain at the least attempt at pressure on them. I have not met with any previous notice of the existence of these spots in Beri Beri, which I believe to be peculiar to the disease.

Tenderness is also sometimes met with over the subcutaneous portion of the peroneal nerve, about an inch below and behind the head of the fibula. The popliteal space is another occasional seat of tenderness. The lexor brevis, sole of the foot also often exhibits a diffuse tenderness. A very common seat of extreme tenderness is the tendo Achillis. There is also frequently great tenderness about the tendon of the quadriceps extensor femoris.

Another almost constant symptom is a sensation of pain referred to the middle and lower part of the sternum. It appears early in the history of the case, while the patient still walks about and possesses a considerable amount of muscular power. It appears to give the patients great trouble. Associated with it is sometimes a suffocating sensation in the chest. One patient with this symptom suffered from very alarming attacks of severe syncope ; he was able to walk. Shortness of breath on comparatively slight exertion is sometimes present. Vomiting occasionally occurs, but it is not common.

The heart usually presents changes to physical examination. The cardiac impulse is not, in mild cases, displaced, but it is usually less forcible than normal. The percussion dulness of the heart in many cases is increased towards the left. On auscultation, systolic murmurs are found to be extremely common. The commonest murmur is one heard in the tricuspid area, presenting a peculiarly harsh character. Murmurs also are common at the base, and they are sometimes heard in the mitral area. The murmurs usually disappear after a short period of treatment by rest in bed in hospital.

The pulse in these cases presents nothing unusual except a tendency to softness. The effect of exertion on the pulse was not observed.

In the acute cases the area of cardiac dulness is enlarged in all directions, especially upwards and to the left, and there is a diffuse, wavy pulsation over the whole præcordia. The cardiac pulsations are extremely irregular, both in force and rhythm. There may be a few slow beats, then a series of frequent feeble pulsations, or a more persistent irregular galloping. Proper auscultation of the heart sounds is impossible, in these grave cases, owing to the restless jactitation of the patient, and the short, noisy, panting respirations cast another difficulty in the path of the observer. The extreme weakness, frequency and irregularity of pulsation, add to the difficulty. Murmurs probably would be heard as they were before the urgent symptoms developed.

The pulse in acute cases corresponds with the condition of the heart. It becomes feeble, increased in frequency, and irregular in force and rhythm. As the case goes on, the pulse becomes still weaker, smaller, and more frequent, till almost imperceptible, and finally disappears in the wrist.

The respiration in chronic cases calls for no particular remark, but in acute cases it becomes frequent, shallow, and panting, and markedly wanting in force and depth. In the cases I have seen, the percussion sound over the lungs has remained clear, and the auscultatory sound has shown harsh and loud breathing, especially at the bases. I have not distinguished moist sounds, though they should be heard in these cases, especially towards the end.

In acute cases the liver dulness is found to be increased downwards, and may fill up the whole of the epigastrum, and project below the margin of the thorax on the right side. The liver can be easily palpated in this position. In the epigastrum the patient experiences pain and tenderness, sometimes very severe.

The acute cases are characterised and ushered in by the rapid onset of urgent symptoms of dyspnœa. The patient, who has probably been suffering from symptoms such as are found in the more chronic form, finds that he cannot get his breath while lying down and feels great and increasing præcordial pain, and sits up for relief. Within a few hours, or less, the dyspnœa and pain become worse and the patient grows restless in his struggles for breath ; he throws himself about, first to one side, then to the other, or leans forward over a heap of pillows, but never for a minute still. He cannot bear to have any bedclothes on, but throws them off if placed over him, beats his breast, and clutches at his throat in his agony for life. His face, pale or bluish in colour, wears an expression of great distress. The body is covered with a profuse cold sweat. The struggles become feebler towards the end, and at length cease, as the feeble, fluttering heart ceases to beat.

The patient complains of thirst during these urgent symptoms, but on attempting to drink, the fluid may roll out of the mouth unswallowed, owing to loss of the power of swallowing.

In the ordinary chronic cases the body temperature remains normal, with a slight occasional rise of about 1°, but in one or two of the fatal cases it has been raised to over 100°, subsiding at the approach of death to subnormal.

The appetite is not impaired to any notable extent in the chronic cases. In acute cases, the struggle for life absorbs the attention to the neglect of food.

The urine is always normal and the bowels are usually regular.

The intellect is unimpaired throughout. The patient of course becomes oblivious to his surroundings in the distress of the acute cases, but never seems to be delirious.

COMPLICATIONS.

Complications were to be noted in some cases.

One very remarkable case was brought in with all the symptoms of acute meningitis, and considerable elevation of temperature. Contrary to expectation, after a severe illness, he recovered, and went out. There were, with the meningitis, tenderness of the calves and loss of knee-jerk. This patient was re-admitted eight months after with extreme weakness and wasting of the limbs, and acute pain and tenderness in the wasted muscles. He was quite helpless. In addition he suffered from constant severe headache, which nothing seemed to relieve. Muscular power improved while in hospital, but he was discharged, as a chronic case, to an asylum, before he was able to walk.

Another patient was demented, and discharged to the receiving house for the insane. I do not know anything of his previous history.

Another suffered from, gout, and chronic nephritis., He afterwards died. to every appearance both from beri beri and nephritis, the beri-beri predominat

Another had a secondary syphilitic rash on his body.

In another case, a pre-systolic and systolic mitral murmur, together with a very marked thrill, were present. There was no preceding history of rheumatism or scarlet fever. This murmur was no doubt of organic origin, and never subsided. In connection with this case we may remember that endocarditis sometimes occurs in cases of peripheral neuritis, apparently as the result of the same poison which acts on the nerves.

DIAGNOSIS.

The diagnosis is very easy when once the symptoms and appearances are known. If a Chinaman complains that his legs are "too sore," or "too tired," it is almost certain to be a case of Beri Beri. The diagnosis may be regarded as confirmed if there is tenderness of the calf, œdema over the crest of the tibia, tender spots in the usual situations on the dorsal and outer aspect of the foot, and if there is a systolic murmur in the tricuspid area, with pain referred to the sternum.

I consider the last four symptoms to be diagnostic of the disease and to distinguish it characteristically from cases of peripheral neuritis of different origin.

As I have already stated, the disease has been missed, and taken for locomotor ataxia, dyspepsia, etc., but these mistakes are difficult to make, even without an interpreter.

From locomotor ataxia the disease is diagnosed by the tenderness of the calves, absence of lightning pains, normal pupil reactions, and by the absence of the characteristic ataxy in the gait. It is possible of course to have ataxy in peripheral neuritis closely resembling that of locomotor ataxia, but I have never seen anything of the kind in Beri Beri. The knee jerk also is lost in locomotor ataxia, but not always in peripheral neuritis when able to walk.

In chronic rheumatism the pains are in the joints, which probably present obvious changes, and when accompanied by muscular wasting, the myotatic irritability is exalted, the knee-jerk increased, and rectus or foot-clonus sometimes obtained.

Dyspepsia is sometimes diagnosed on the assumption that a pain in middle or lower part of sternum is most likely due to that cause, no further examination being made, and any other symptoms being neglected.

I have also several times known the disease mistaken for lead-poisoning, but in lead-poisoning the arms are attacked first and most severely by neuritis, and the supinator longus is not affected, and there are absence of other signs of lead-poisoning, such as colic, and the blue line on the gums.

The diagnosis from neuritis of alcoholic origin must depend chiefly on the history and the surrounding circumstances of the case. The pain referred to the sternum is present in the slight cases of Beri Beri, and is relatively uncommon in alcoholic neuritis, even when advanced. In advanced cases the electrical reactions of the facial muscles will probably afford means for diagnosis. To an experienced observer, moreover, the facial aspect frequently conveys valuable information as regards the probability of the existence of an alcohol habit. The so-called cases of rheumatic polyneuritis are in my experience very uncommon in Sydney. The diagnosis must rest on the history and surrounding circumstances. The same applies to post-influenzal polyneuritis, also uncommon, which sometimes assumes a very serious form.

Malarial neuritis, of which I have not had personal experience, is said only to be manifested in the legs, and would thus be distinguishable.

In the acute cases there will probably be obtainable a history of weakness, or pain, and some tenderness in the legs. A history of swelling in the legs does not give much help in diagnosis, from the occurrence of the same in other diseases from which acute Beri Beri has to be diagnosed. The facial appearance is characteristic, and different from that usually found in Bright's disease and the common forms of heart disease. There is a look of intense anxiety, and the countenance is perhaps more vividly expressive than is often noticed in these diseases. The puffiness under the eyes is wanting, and the skin is apt to be bathed in a cold sweat. In cases of valvular heart disease with failing compensation, there will be certainly great œdema of the legs and probably a considerable amount of evident ascites. In the cases of acute Beri Beri seen at the Sydney Hospital, œdema of the legs has been extremely slight and only obtained by pressing against the surface of the tibia. I am aware that œdema of the legs in acute Beri Beri is sometimes very marked, but its extremely slight amount in many cases is against a diagnosis of valvular heart disease. In acute and subacute Bright's disease there is also marked œdema of legs, œdema of the back, and all the lax tissues, with more or less moderate ascites, with an increased tension of pulse, and albuminuria with casts. In Beri Beri the pulse tension is much lowered and there is no albuminuria, unless of course the two diseases coexist.

The disease with which acute Beri Beri is most likely to be confounded is acute pericarditis with effusion. In the latter disease the pulse is feeble, frequent, and irregular in force and rhythm, and the physical signs of pericardial effusion are present, with depression of the liver dulness, combined with pain in præcordial region, panting respiration, anxious face, and jactitation. In addition to this a history of pains in the legs may induce one to think of preceding rheumatism. But in the cases of Beri Beri I have seen, the onset, course, and termination of the acute symptoms have been far more urgent and rapid than occurs in pericarditis. In addition to this a friction sound is usually easily audible on auscultation in pericarditis. In acute Beri Beri, the antecedent pains will be found to have existed in the calves, together with weakness of the limbs; no joints will be swollen, but the calves may be tender. In pericarditis the temperature will probably be considerably raised.

MORBID ANATOMY.

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The morbid anatomy, as revealed by post-mortem examinations, refers only to acute cases, and is gathered from the results of four examinations made at the Sydney Hospital by Dr. Sydney Jamieson, at all of which I was present. There have been autopsies on about two other cases, but one was not recognised at the time, and the other suffered from coincident organic disease, and for this reason they are left out of account.

The Chinese object very strongly to post-mortem examinations and this throws a great difficulty in the way of pathological investigation.

The body was spare in the second case, well nourished in three others. No œdema over the tibia was present in the second and third cases, slight œdema in the other two. In the third case the body had a somewhat anasarcous appearance as a whole, but there was no pitting on pressure.

On opening the thoracic cavity, and examining the lungs, they were found in every case deeply congested and œdematous. The first case presented numerous small sub-pleural petechial hæmorrhages between the lobes, of recent origin, and the same case presented in the right lung two or three deeply congested wedge-shaped areas, but still containing some air. These appeared to be very recent infarcts.

The fluid contained in the pleural sacs was not abnormally large in quantity.

The pericardial sac was more or less distended by fluid in every case. In the second case the amount of fluid was not very great, but in the third the distension was extreme, the pericardial sac measuring 15½ inches from apex to base, and 15 inches transversely, and containing about 18oz. of clear, straw-coloured fluid; in this case also the fat over the pericardim was extremely œdematous. The case which presented sub-pleural petechiæ had the same beneath the epicardium. No signs of pericarditis existed in any.

The heart in every case was very much distended, the right side being especially concerned. The weight was from 16 to 18½oz. On section, general hypertrophy of the muscular tissue presented itself. The tissue was very pale and lacked firmness. In the first three cases the musculi papillares of the left ventricle showed signs of fatty change. The cavities of the right side of the heart were filled by dark, more or less fluid blood. In the first the left ventricle was empty, in the other cases it contained blood. Thickening of the endocardium of the left auricle was noted in the first and third cases. The valve segments were all healthy, but the mitral and tricuspid valves abnormally large.

The liver was always congested, and in the first, third, and fourth, especially the third, there was marked enlargement. Dr. Jamieson made the remarkable discovery, in the second case, of the existence of specimens of the *Distoma sinense* in the gall ducts. The parasite was not looked for in the first case, but it was found to exist in the three others. One of the patients was a Japanese stoker from a steamer in the port, another came from a cabinet maker's shop, and another was a gardener. It was found only in the gall ducts, and not in the gall bladder. In this place it is due to mention that in the first three autopsies the body fluids were noted to be slightly bile-stained. In the first and fourth case the walls of the gall bladder were œdematous. The bile was always of a dark olive green colour. The kidneys were normal in all, but for some congestion, chiefly in the pyramids or in the boundary area.

The spleen varied in size, being 11oz. in the first case, 4½oz. in the second, 17oz. in the third, and 9½oz. in the fourth. In all it was of normal consistence and of a dark plum colour. In the fourth case there was about a pint of fluid in the peritoneal cavity.

Portions of the peripheral nerves supplying the limbs, and the vagus and its branches, were hardened and treated with osmic acid, and then subjected to microscopic examination, with the result that degenerative changes were demonstrated in all the specimens examined, thus confirming the diagnosis arrived at from consideration of clinical facts.

The spinal cord has not yet been examined microscopically.

Attempts to obtain micro-organisms have not yielded satisfactory results. In the third and fourth cases, tubes inoculated with pericardial fluid and incubated, remained uniformly sterile. In the first case, unfortunately, no search for micro-organisms was made ; in the remaining three, films of blood and of pericardial fluid were stained and examined. In the second and third, nothing was found, but in the fourth micrococci were observed in pericardial fluid. The value of this observation is vitiated by the fact that tubes inoculated with every precaution from the same case remained sterile. Dr. R. T. Paton and Dr. G. H. Taylor have found bacilli, (?) staining deepest at the ends, in several cases belonging to the Coast Hospital, both in blood and, in a fatal case, in pericardial fluid.

It is evident that further investigations are required.

PATHOLOGY.

The disease as one manifesting itself by a symmetrical peripheral parenchymatous neuritis, is to be regarded as due to an altered blood-state, caused by the entrance of some poison into the circulating medium which exerts a selective action on the parenchyma of the peripheral nerves.

This disease appears to belong to the miasmatic class. Several people living in one house may become affected. If these people leave the house and go to a healthy locality, the disease goes no further, and the patients tend to recover. There is no evidence that the disease can be directly transmitted from one patient to another.

Many strong considerations exist to induce us to the hypothesis that the virus is a specific living contagium, or micro-organism of some kind. Among these are the apparent confinement of the virus to certain localities and dwellings, its association with peculiar physical conditions of existence, its predilection for one race, and its somewhat greater prevalence at one season than at another. It is to be remarked also that the disease has only become very prevalent during the last three or four years, though the conditions otherwise existing among the Chinese have remained the same ; pointing to the introduction of a new factor in disease presenting the power of increase.

So far as the disease is known in Sydney, the life-history of the virus has seemed in its course to have had some peculiar connection with man, especially with the Chinese race, which it has followed and attacked exclusively. Analogy with other diseases only strengthens the argument in favour of its specific nature.

It is true that in Sydney the virus has not yet been separated and proved capable of causing the disease, and no other, when absorbed by a healthy person, but Pekelharing and Winkler claim to have separated a characteristic organism, in the Beri Beri of the Dutch East Indies, capable of causing peripheral neuritis in rabbits. Other investigators in other countries have also described various organisms. The results obtained in Sydney are conflicting and not very satisfactory.

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The curious phenomenon of the discovery of a peculiar liver fluke in three consecutive cases of Beri Beri is very remarkable. There is at present no evidence to prove that liver fluke is the source of the toxic material. The fluke is now being sought for as a routine practice in the bodies of Chinese, but only one autopsy on a Chinese patient has taken place since the last fatal case of Beri Beri, and in this no fluke could be found. It may, however, turn out to be not really uncommon in patients not suffering from Beri Beri, is presence having been formerly overlooked. This has proved to

The weakness, wasting, tenderness, altered electrical reactions, and derangement of sensation in the limbs are all explained by the peripheral neuritis which has been demonstrated to exist in such cases as have afforded opportunity for post-mortem examination.

The pain in the region of the sternum, with the enlargement and dilatation of the heart and development of a heart murmur are explained by a similar derangement of the vagus nerve, interfering with its normal performance of function. In the more severe cases, where the heart shows the signs and symptoms of acute dilatation, and the pericardial cavity becomes more or less distended by dropsical effusion, accompanied by increasingly feeble respiratory power, a more grave affection of the vagus has taken place, together with general involvement of the nerves associated with the muscles of respiration. The pronounced difficulty in swallowing which I have noted, is due to involvement of the branches of the vagus associated with the æsophagus and perhaps other muscles. This affection of the act of deglutition is worthy of remark, as it has not previously been recorded as occurring in any case of multiple neuritis.

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The usually small amount of œdema met with in the legs, chiefly noticeable over the crest of the tibiæ, and the tendency to profuse cold sweats, is due to a disordered condition of the vaso-motor apparatus, which has been disturbed by the presence of the toxic influence in the circulation. Dropsy of the legs of cardiac origin may be expected to occur in cases that survive for some time in spite of considerable vagus degeneration, but such cases have not yet been seen at the Sydney Hospital.

The downward increase in the amount of liver dulness seen in acute cases is due partly to enlargement from passive congestion, the result of backward pressure from the heart, but it is chiefly due to depression of the organ by the dilated right heart and distended pericardium. The congestion and œdema of the lungs seen post-mortem is due partly to increased backward pressure from the heart, and partly to the enfeeblement of the respiratory act.

The tender spots on the dorsal and outer aspects of the foot are probably due to the superficial position of the underlying nerves, which are tender through involvement of the nervi nervorum of the sheath.

PROPHYLAXIS.

In considering the measures advisable for the prevention of the origin and spread of the disease, we are early brought to recognise the fact that the manner in which the Chinese live is one particularly well suited to the spread of any communicable disease which may make its home in their dwellings. A large number of people live, eat, and sleep in one small, dirty unventilated room or "den." The absence of cleanliness and of a free current and change of air prevents the removal and favours the accumulation of any disease germs present. The overcrowding allows a large number of persons dwelling under conditions likely to depress the resistive power of the individual, to become exposed to the poison, and absorb it, either in respired air, or contaminated food and drink.

The prophylactic measures therefore suggested are a reform in the hygienic arrangements of the dwelling rooms by which cleanliness is carefully attended to, and suitable ventilation obtained. Each inhabitant should have a much larger cubic space of air for his share, and means for its proper renewal provided.

When a case of Beri Beri, however mild, is found to have arisen in the house, the patient should be isolated, and the place should be thoroughly cleaned out, scrubbed, and fumigated, and proper ventilation insisted on. No rubbish should be allowed to be about the place, as it may form a harbour for disease germs. It will be unnecessary to do more than mention the importance of efficient drains and drainage. The possibility of the conveyance of the disease by clothing and furniture should be thought of, and the contingency provided against.

TREATMENT.

The first indication in treatment is the removal of the cause or causes, determining or predisposing. These have been discussed when considering the ætiology and pathology of the disease. As there is reason to believe that the disease represents a toxæmia due to a specific miasm which infects certain houses or places, the first and by far the most important step is the removal of the patients to healthy surroundings. If this be done the patient is prevented from receiving any more of the toxic cause with which he has previously been poisoned. The absorption of the cause probably goes on continuously as the patient remains exposed to its influence, the manifestation of the disease varying in severity according to the amount of the dose received, and the resistive power of the patients to its influence.

The next two indications are, firstly to find a specific by the administration of which to the patient the virus may be destroyed. This specific is not yet discovered. It is possible that it may yet be found, and it will probably be an antitoxine analagous to those employed in the serum treatment of tetanus and diphtheria. Secondly, we must place the patient's organism in the most favourable condition for resisting the disease. This, after having removed the patient to an uninfected locality, consists in looking after the general health, and the treatment of symptoms as they arise.

In beginning the treatment of these cases, whether mild or chronic, after fulfilling the first indication, I regard a period of rest in bed as of the highest importance, and proved efficacy. This should be omitted in no case, however mild it may seem. In the slight cases the patient may be allowed up at the end of a week ; in other cases the period must be longer. Attempts to drive into functional activity the suffering nerve fibres before even the destructive influence of the virus has yet had time to cease, can only do harm. When the more or less degenerated nerves may be expected to be on the road to recovery, a reasonable amount of mild exercise probably does good.

If there are any signs of dyspnæa the need for rest in bed is still more urgent.

Under treatment by rest in bed alone, œdema will disappear, pain lessen, and heart murmurs vanish. When the weakness has reached a certain stage, of course rest in bed is insisted on by nature.

The drug treatment of these cases has been various ; Strychnine, with Nitro-hydrochloric Acid and Compound Infusion of Gentian has been often used, so has Easton's Syrup, also Iron, with Sulphate of Magnesia and Dilute Sulphuric Acid, in the form of the ordinary Mist. Ferri Aperiens of the hospitals, and Arsenic, too, has been tried. I cannot say that it has mattered much, if at all, what drug was taken, or whether no drug was used. The rule is, that if a patient comes into the hospital, he improves equally well under any, or perhaps even no drug.

The pain frequently calls for direct treatment, and for this there is no better drug than Antipyrin. It may be necessary in some cases to employ opium or morphine in some form, but its use is to be avoided when possible, lest a habit of taking it should be formed which the patient will not, or cannot, throw off. Cannabis Indica may be tried instead, sometimes, with benefit.

The practice of counter irritation to limbs or back is only mentioned to be condemned, as utterly contra-indicated, and much more likely to do harm than good.

The food should be digestible and nourishing. The digestive powers are not strong, and the disease needs supporting treatment.

Attention should be paid to the position of the limbs in helpless cases. The "dropped foot" position should be remedied by placing a suitable support against the feet. Neglect of this precaution might lead to a persistent deformity.

With regard to the use of electricity in this disease, it is necessary to emphasise the uselessness of faradism as an agent for restoring degenerated nerve fibres. The routine employment of the faradic current for the paralysis of peripheral neuritis is irrational and unscientific, and unwarranted by any clinical evidence of its value.

On the other hand, the galvanic current is much to be recommended in helpless cases, in order to preserve the nutrition of the muscular fibres as much as possible by causing them to contract in obedience to an artificial stimulus in the absence of the natural nerve-stimulus. In cases possessing fair muscular power, electricity may be dispensed with, as the patient is still able to use the natural stimuli for contracting and exercising the muscle fibres.

I do not think that treatment is very hopeful in the fulminating cases I have described. For the urgent cardiac symptoms the hypodermic injection of ether and of caffein have each been used, without the slightest appreciable good effect. Drug treatment in these cases should be hypodermic, for anything swallowed will probably remain for a considerable time unabsorbed. Moreover, in these cases, the power of swallowing may become interfered with owing to œsophageal paralysis, and fluids taken cannot be swallowed, but run out of the mouth. Counter irritation by mustard to the præcordia has been tried unavailingly. The patient should be kept as warm as possible. It is no use heaping up clothing for he will throw it off, and will probably also kick hot water tins out of the bed if strong enough. The most important indication is suggested by the efforts of the patient for breath; he should have as much fresh air as possible. The thirst complained of may be lessened by frequent moistening of the mouth. I think that paracentesis of the dropsical pericardial cavity would be useless, in view of its cause.

PROGNOSIS.

The prognosis of the more chronic cases, if placed under proper treatment, is good. The development of acute symptoms should lead to a very grave prognosis. If the acute symptoms are rapid in their onset, so far as present experience goes, the prognosis must be absolutely hopeless, and death can be expected within 24 hours of the onset of serious symptoms.

In the slighter chronic cases the patient may be right in from two to three months. When advanced paralysis has set in of course the case is much longer, but considerable variation is shown in the rapidity of recovery, which takes place in from six to twelve months.

After removal of the patient from the place in which he contracted the disease, improvement is not always immediate, for he may be able to stand or walk a little for the first two or three days, and then become helpless. This is due to the influence of the virus absorbed before coming under the new conditions, which has not yet worked itself out. According to present experience, if he has not become worse during the first few days, the danger of his becoming so is past.

If the patient is re-exposed in any case to infection, recovery is impeded, or a relapse takes place. If the patient continues to reside in the affected locality, though the amount of virus absorbed may not be sufficient to cause enough weakness, swelling, and pain, to prevent his continuing at work, he remains a sufferer in this way till an exacerbation renders him useless, when he comes to hospital, and there, under the more favourable conditions existing, he recovers. If he goes back to the same place the disease is likely to again seize him, and he may be a sufferer in greater or less degree for years.

The symptoms remain longest in the legs, the parts first and chiefly affected.

CONCLUSION.

In concluding this paper, I desire to say that it is not intended to be a complete account of Beri Beri as a disease, and a summary of the present state of knowledge in regard to it, but it is only such an account as I am able to render as the fruit of individual experience. It follows that there are many things left out which might otherwise have been mentioned, but on the other hand, I think I can say with some degree of confidence, that my enquiries into the subject have enabled me to bring forward one or two observations not before recorded in the literature of the disease.

CYRIL ERNEST CORLETTE.

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SOME NOTES ON THE URINE IN BERI-BERI.

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The following notes are not put forward as being in any way exhaustive, but rather to attract the attention of those who may have other cases of peripheral neuritis under their care (arsenic, alcohol, diphtheria, etc.) How far such different forms of "nerve disease" may be distinguishable by the degree to which the metabolism of the individual may be upset, is a point yet to be determined. It is possible that some aid in establishing diagnoses may be obtained by attention to such matters.

It has long been known, as from the work of Scheube[1] that the excretion of urea and phosphates is much diminished in beri-beri; the figures set out in the accompanying table serve to confirm this point. It will be observed that the figures for urea are extraordinarily low in certain of the cases, so low indeed that it was not until I had made control observations on the healthy, that I was satisfied that there might not have been some error of calculation or of observation. The possibility of some tampering on the part of the patients can be excluded by reference to the proportions of other constituents.

The patients were of three races—Chinese, Tamil (Madras Indians), and Sikh. It will be observed that the Chinese controls gave figures which were comparable to the ordinary physiological standard. Such, however, is far from the case with the control Tamil cases, and it may be doubted whether these men were really in a normal condition, apart from the trivial matters for which they were under hospital treatment. It should be stated[2] that in the Malay States, as Braddon and others have insisted, the Tamil escapes beri-beri in his home life so completely that cases are but rarely seen in the hospitals. The insusceptibility, or rather non-acquisition, of the disease is even more pronounced in the Sikh, and, further, usually endures during confinement in gaol, so that beri-beri in a Sikh is most exceptional. In the case of the Tamil, it may be suggested as a possibility that for some reason their nerves are more sheltered from the action of the beri-beric poison, so that they only suffer from a disturbance of metabolism—a "beri-beri sine neuritide." Naturally the control cases are much too few in number to establish such a possibility as a fact, but if it leads to a more complete knowledge of the metabolism of the Tamil, the suggestion will be justified.

DIET.

In respect to diet these control Tamil cases were perhaps on a more liberally albuminous diet during their stay in hospital than in their life outside; for they had 4 oz. of salt fish four times, and 2 eggs three times a week, with vegetables, curry stuffs, and rice. The Chinese hospital patients have 4 oz. of dried fish or meat each day, with rice and vegetables. The diet of the prisoners contained 6 oz. of meat or fish a day in the case of the long-sentenced men, but none in the case of the short-sentenced men. Two cases with extraordinary low urea values (Table Nos. 6 and 17) had been on bread and water for the twenty-four hours during which the urine was collected. The question of malingering naturally has frequently to be taken into account in gaols, and in these two cases the signs of beri-beri were not of severe type, though the diagnosis seemed to be confirmed by the low urea figure, which is below a starvation amount.

UREA.

I did not have the good fortune to examine a case of sudden death shortly before the time of decease, but it is probably not unreasonable to conclude that an individual who is only excreting a fifth or a sixth of the proper amount of urea might be prone to the onset of the sudden death which is so commonly unanticipated in the disease; nor again is there cause for surprise that these two patients complained of not feeling well, although neither cardiac distress nor paralytic symptoms were prominent. They had no albuminuria.

The question arises whether the diminution of the urea is due to a locking up in the tissues, to a deficient removal by the kidneys, or to an actual diminution of output by the effective organs.

It may be stated here that none of the samples tested showed the slightest trace of albumen; this, coupled with the comparatively normal amounts of uric acid and kreatinin, points to the conclusion that the kidneys cannot have been seriously at fault. Moreover, the marked diminution of the phosphates and sulphates confirms the idea that the production is really at fault.

The two following direct' observations are opposed to the idea of a locking up of already-formed urea in the body; though the readings are perhaps a little high, it is to be remembered that the sources were *post mortem;* and that there may have been other substances yielding nitrogen with hypobromite.

1. Residue of alcoholic extract of 100 grams of blood after removal of cholin-like bodies, etc., by means of alcoholic platinum chloride, yielded nitrogen corresponding to 0.0308 grams of urea, that is, 0.3 per mille.

2. Residue of 40 grams of pericardial fluid similarly treated gave nitrogen corresponding to 0.0112 grams of urea or 0.28 per mille. Hammarsten[2] gives the normal urea content of the blood as 0.2 to 0.15 per mille.

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No.	Nationality.	Condition.	Date.	24 Hours' Urine in c.cm.	24 Hours Urea Grams.	24 Hour Uric A Grai
—	European	Normal (Schäfer's Text-book)	—	—	33.180	0 53
†1	Chinese	Healthy	16/10/02	1,180	30.710	0.5
†2	,,	,,	16/10/02	1,000	26.117	0 7
‡3	,,	Recent beri-beri	4/9/02	1,280	14 660	Very l not weigh
‡4	—	,,	19/12/02	1,670	11.110	0.10
†5	Chinese	,,	16/9/02	1,600	18.660	Less th 0.35
†6	,,	Beri-beri ? recent	16/9/02	1,600	4.480	Less t 0.11.
†7	,,	Recent recurrent beri-beri; critical urination	27/10/02	4,400	15.750	0.2
†8	—	,,	3/11/02	2,820	27.470	—
‡9	Chinese	10 months' beri-beri	31/10/02	645	8.300	0.4
‡10	Tamil, control	Synovitis	19/12/02	1,640	10.850	0.21
‡11	,,	Ulcus cruris	24/1/03	1,610	9.930	1.05
‡12	,,	,,	24/1/03	1,590	9.350	0.920
‡13	,,	"Rheumatism"	24/1/03	840	6.740	—
‡14	,,	Fistula in ano	24/1/03	1,200	9.790	0.5
§15	Tamil	Recent beri-beri	8/10/02	1,640	10.060	0.4
§16	,,	Recent beri-beri, very oedematous	3/11/02	2,700	8.320	0.5
§17	,,	Incipient beri-beri	8/10/02	1,245	4.060	0.54
§18	Sikh	Recent beri-beri	2/10/02	720	9.950	0.0
§19	,,	,,	8/10/02	1,140	6.110	0.11
§20	,,	,,	14/10/02	940	12.080	—
§21	,,	,,	27/10/02	1,630	6.650	0 5
§22	,,	,,	7/11/02	1,600	3.890	0.04

* Kreatinin by zinc method. † Prisoner, long sentence.

24 Hours' P_2O_5. Grams.	24 Hours SO_3. Grams.	24 Hours Conjugated SO_3. Grams.	24 Hours' SO_3 after Oxidation. Grams.	24 Hours' SO_3 of Neutral Sulphur. Grams.	Ratios Uric Acid / Urea.	Kreatinin / Urea.	P_2O_5 / Urea.	SO_3 / Urea.
3.160	2.010	$\frac{1}{10}$ of total SO_3	—	$\frac{1}{5}$ of total S	$\frac{1}{66}$	$\frac{1}{36}$*	$\frac{1}{10}$	$\frac{1}{16}$
2.863	1.986	0.163	2 400	0.420	$\frac{1}{60}$	$\frac{1}{18}$	$\frac{1}{11}$	$\frac{1}{16}$
2.699	1.450	0.070	1.731	0.271	$\frac{1}{37}$	$\frac{1}{18}$	$\frac{1}{10}$	$\frac{1}{18}$
1.740	—	—	—	—	—	$\frac{1}{19}$	$\frac{1}{8}$	—
—	—	–	—	—	$\frac{1}{111}$	—	—	—
1.180	—	—	—	—	$\frac{1}{60}$	$\frac{1}{19}$	$\frac{1}{17}$	—
0.620	—	—	—	—	$\frac{1}{46}$	$\frac{1}{6}$	$\frac{1}{7}$	–
0.970	1.060	0.086	—		$\frac{1}{60}$	$\frac{1}{9}$	$\frac{1}{17}$	$\frac{1}{16}$
1.950	2.330	0.159	—	—	—	$\frac{1}{13}$	$\frac{1}{14}$	$\frac{1}{12}$
0.750	—	—	—	—	$\frac{1}{20}$	$\frac{1}{7}$	$\frac{1}{11}$	—
1.632	—	—	—	—	$\frac{1}{64}$	—	$\frac{1}{7}$	—
—	—	—	—	—	$\frac{10}{99}$	$\frac{1}{10}$	—	—
0.860	—	—	—	—	$\frac{1}{10}$	$\frac{1}{7}$	$\frac{1}{11}$	–
—	—	—	—	—	—	$\frac{1}{7}$	—	—
—	—	—	—	—	$\frac{1}{19}$	$\frac{1}{8}$	—	—
.860	—	—	—	—	$\frac{1}{24}$	$\frac{1}{14}$	$\frac{1}{11}$	—
—	0.970	0.056	—	—	$\frac{1}{13}$	$\frac{1}{7}$	$\frac{1}{17}$	$\frac{1}{9}$
0.550	0.305	—	0.410	0.105	$\frac{1}{8}$	$\frac{1}{4}$	$\frac{1}{7}$	$\frac{1}{13}$
.760	—	—	—	—	$\frac{1}{30}$	$\frac{1}{16}$	$\frac{1}{13}$	—
.580	0.760	—	0.869	0.109	$\frac{1}{60}$	$\frac{1}{6}$	$\frac{1}{10}$	$\frac{1}{8}$
.880	—	—	0.828	—	—	—	$\frac{1}{7}$	—
.590	0.530	0.023	0.633	0.103	$\frac{1}{13}$	$\frac{1}{8}$	$\frac{1}{11}$	$\frac{1}{13}$
—	—	—	—	—	$\frac{1}{100}$	—	—	—

short sentence. ‡ Patient in district or general hospital.

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OTHER CONSTITUENTS.

In contrast to the urea the kreatinin, as estimated by S. Johnson's process, may be hardly decreased, indeed it is proportionately increased in nearly all of the cases.

Whilst both the sulphuric and the phosphoric acids show absolute diminution the increase proportionately to urea is more marked in the case of the former than of the latter ; it will be remembered that Scheube insists that the phosphoric acid is relatively increased in the majority of cases. Mott and Halliburton have shown that during degeneration nerves lose a considerable amount of their phosphorus, but their degenerated condition can hardly be the direct cause of the diminished excretion in that the phosphoric acid obtainable from the whole of the human nervous system is estimated to be only 12 grams (Voit[4]), whilst that of the muscles is given as 130 grams.

The proportions of the conjugated sulphuric acids and of the neutral sulphur were not found to be affected in the first few cases, so that further estimations were deemed to be superfluous.

Several estimations of the purin bodies were made, but owing to various accidents the following only were brought to conclusion. Still they do not appear to be of much importance in the elucidation of the disease.

Estimation of Purin Bodies.

No. (vide Table).	7	21	4	10
Ammonia soluble ...	0.067	Lost	0.037	0.059
Ammonia insoluble ..	0.032	0.009	0 008	0.005
Total	0.099	——	0.045	0.064
Uric acid	0.283	0.534	0.105	0.210

Some further inquiry was made to determine whether any other substances of interest were to be found. It is to be regretted that the means for the estimation of the total nitrogen were not available. Some attempts were made to get figures for the hippuric acid, but no useful figures were obtained though the substance was readily demonstrable.

Some attempts were made to isolate bodies of a basic nature from the urine. In demonstrating the presence of cholin or cholin-like substance in the blood or other body fluids it was found that the syrupy, highly alkaline residues obtained by alcohol extraction yielded up a substance to benzol which gave a double salt with platinum chloride crystallizing in octahedra from 15 per cent. alcohol. Thus the difficulty of employing sufficiently anhydrous alcohol in so moist a climate was avoided, and the presence of potassium salts could be definitely excluded. The shake-out method with benzol was consequently applied to several urine samples both before and after alkalinization with quicklime. A number of double salts with platinum (gold salts were only made with the "cholin" of the blood, etc.) were obtained, but, like Mott and Halliburton, I failed to get any octahedra suggestive of cholin. The only substance worthy of mention was one whose platinum compound was of a brilliant orange-vermilion colour, and was soluble in strong alcohol. Marked quantities were obtained from the beri-beric cases, and but mere traces in the few controls. The quantities obtained were not sufficient for further examination. The scarlet body usually crystallized in minute octahedral crystals.

METHODS ADOPTED.

Since in the tropics conditions are not always favourable in respect to materials and apparatus, a few words on the methods employed may be added in order that the value of the estimations may be judged. In all cases the urine was measured and then filtered. It was directed to be passed directly into large stoppered bottles into which a few drops of toluol had been placed to prevent putrefactive changes; the twenty-four-hour periods were arranged from 6 a.m. to 6 a.m. to avoid delay fer the like purpose. Albumen was tested for and found absent before proceeding.

A good delicate balance was available, and gravimetric methods had to be adopted in most cases; these had the disadvantage of limiting the number of observations.

Urea was estimated with freshly-made hypobromite solution, the quantity taken being 5 c.cm. and repeated on 10 c.cm., where the reading was very low; with normal urines only 2.5 c.cm. could be used on account of the size of the only available burette. The same measuring cylinder was used throughout, and after draining it was rinsed out with water into the testing tube to avoid loss. Temperature correction to 60° F. and 37 1 c.cm. nitrogen taken as equivalent to 0.1 g. of urea.

Kreatinin.—400 c.cm. of urine were treated after S. Johnson's method, about a teaspoonful of potassic acetate and 100 c.cm. of saturated corrosive sublimate being used. After the immediate filtration the mixture was stood for forty-eight hours and filtered; after this period a precipitation of crystalline flakes occurred. The figures under kreatinin (or better perhaps "Johnson precipitate") are reckoned at 19 per cent. of the mercury compound. It should be added that the figures quoted from Schäfer are the absolute kreatinin estimated by more exacting methods,

Uric acid was precipitated by Hopkins's method with excess of ammonic chloride which itself had been recrystallized to remove particulate matters; the precipitate was taken direct upon a tarred asbestos wool filter by a suction pump or syringe. After washing with saturated ammonic chloride and a little spirit, the tubes were left to stand with a few drops of 10 per cent. HCl in spirit, whereby the uric acid was liberated in crystalline form. Later the uric acid was washed with a little water and spirit, and dried eventually in partial vacuum over $CaCl_2$ and quicklime to constant weight; 100 c.cm. were used for each titration. There did not appear to be any loss in the wash filtrates, as judged by the murexide reaction.

Phosphoric Acid.—The only available mode of estimation was as magnesium pyro-phosphate. A sulphate of magnesia mixture was used, the precipitate being taken up with dilute sulphuric acid, and reprecipitated with ammonia; 200 c.cm. of urine were used in the determinations.

Sulphuric acid was taken with samples of 100 c.cm., which were boiled respectively with 5 c.cm. of acetic or hydrochloric acid (the former subsequently with HCl), and precipitated with barium chloride. The weighings were direct without incineration.

Oxidation for the *neutral sulphur* was done by cautiously adding excess of permanganate day by day until a permanent pink colour was obtained.

The *purin bodies* were doubly precipitated with ammoniacal silver nitrate after removal of phosphates and intermediate removal of uric acid with dilute sulphuric. After reduction of the silver compounds with H_2S they were classified into ammonia soluble and insoluble.

The estimation of sodium, potassium chlorides, etc., was not attempted.

My thanks are due to Drs. Travers, Gimlette and McClosky, of the Malay States Service, for the use of their cases and other help. I am also indebted to the Government of the Malay States for the use of the laboratory at Kuala Lumpur, until they behaved with such discourtesy that it was not possible to remain as a guest of such inhospitable hosts: Captain Rost kindly offered facilities in Rangoon, but unfortunately the season was not favourable for the study of beri-beri. I must also express my gratitude to Dr. F. Gowland Hopkins for much advice.

SUMMARY.

Curtly put, the above notes show that the metabolism in beri-beri is seriously diminished. The amounts of urea, phosphoric, and sulphuric acids may be very greatly reduced; it is suggested that the contributing organs, for example, liver, are seriously disturbed in their output, which is in accordance with the fact that patients complain of illness before the onset of marked symptoms of the involvement of the peripheral nerves.

The conjugated sulphuric acids and the neutral sulphur do not appear to be proportionately diminished.

The purin bodies do not seem to be of great interest in beri-beri; as might be anticipated, they were abundant in the critical urination of a highly oedematous case.

In a number of Tamils, on comparatively liberal diet, in whom no beri-beric symptoms were detected, the excretion of urea and phosphoric acid was found to be remarkably low, though their uric acid was high.

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P. 129
5
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ON BERI-BERI.

By Stuart Eldridge, M.D.,

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The medical profession of San Francisco must naturally feel some interest as to the clinical history and pathology of the anomalous and little known disease, Beri-beri, recently introduced by the agency of the Brazilian man of war, Vital d' Olivera, especially as the accounts given by the few medical authors who have noticed the disease are brief, unsatisfactory, and often but a rehash of the crude and hasty observations of the older writers upon the diseases of India.

So many instances are known in which diseases have been transplanted to virgin soil, there to flourish with a virulence equal to or greater than that exhibited in their native habitat, this being true even as regards some diseases not generally acknowledged to be contagious; that the fact of the importation of a large number of cases of a malady hitherto unknown in the United States but recognized elsewhere as prone to extend, as intractable under treatment as is cholera, and, at least in its severer form almost or quite as fatal as the latter, should certainly afford matter for serious consideration.

For many years, the disease in question was believed to be strictly confined to the far East, i. e. to certain parts of India, and the Malay Archipelago. In 1866, however, Dr. Da Silva Lima, of Bahia, published in an obscure local journal accounts of outbreaks of Beri-beri in several districts of Brazil, in which country he believed the disease to have existed for a considerable period, being known to the local practitioners as the "Morbus innominatus." It was not until 1872, when the papers alluded to were republished in collected form, with other and later observations on the disease, that the existence of Beri-beri at a point so remote from its acknowledged habitat, attracted the attention which the importance of the subject demanded; while the fact of its prevalence in Japan where it is one of the most common and fatal of endemic diseases, is, as yet, almost unknown to the profession at large.

A careful study of the somewhat unsatisfactory literature of the subject, with an acquaintance of nearly ten years with the Japanese form of the disease, known to the natives as Kak'ké, has convinced me that in no essential point does the Beri-beri of India and the Malay Archipelago differ from the "Morbus innominatus" of Brazil, or either from the Kak'ké of Japan.

It is a singular fact, that, although, as we shall see farther on, the conditions in China seem especially favorable to the development of the disease; and although it was known and accurately described in that country about 1321 or even earlier, it has at the present day almost or quite disappeared from the Middle Kingdom. Inquiries as to its presence made by the writer in 1877, and addressed to foreign physicians at the various open ports of China, failed to elicit a single affirmative response. I learn, however, that Dr. P. Manson, of Amoy, so favorably known in connection with his investigation of the parasitic origin of Elephantiasis and its congeners, has during the past two years encountered a few cases which he believes to be of Beri-beri. Granting that Dr. Manson's opinion is correct, the fact remains that the disease is very uncommon in China, at least in those regions known to foreigners.

Of the standard systematic works on medicine which mention the disease at all, the Dictionary of Copland, that marvelous work, considered as the product of the learning and advanced thought of a single man, gives a correct but incomplete account of the symptoms of the Indian malady. Aiken devotes a brief article to it; Woillez, *Dict. de Diagnostic Medical*, Paris, 1870, gives a clear and accurate description of its leading features, while Johnson and Martin in their respective works upon the "Influence of Tropical Climates," delineate the disease as met with in India in the earlier years of the British occupation. With these, and perhaps a few other exceptions, the history of Beri-beri must be sought in papers scattered through the medical and scientific journals and transactions of various European and Asiatic countries.

Among these contributions, as relating to the Japanese disease, may be mentioned articles by Hoffmann, in the Transactions of the German Asiatic Society of Japan for 1872, and by Anderson, in St. Thomas' Hospital Reports, London, Vols. VII and VIII. Of its appearance in the Malay Archipelago, an article by Damman in L'Association Medicale, Paris, 1863, gives an admirable though brief description, together with a tolerably complete bibliography of the subject. As regards Brazil, the original papers of Dr. Da Silva Lima, before mentioned, may be consulted, or, should these prove inaccessible, an abstract of considerable length in the Edinburgh Medical Journal for March, 1873.

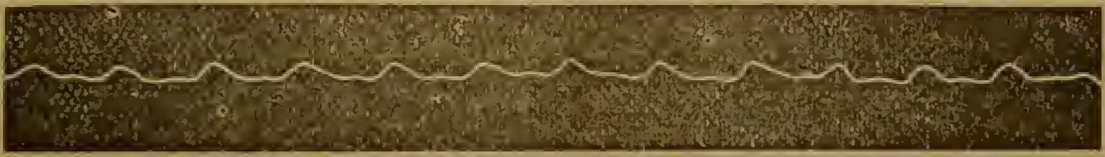
Repeating that the Kak'ké of Japan may be considered as typical Beri-beri, I will endeavor to give some idea of the clinical history of the disease, with a notice of what is known or suspected as to its etiology, pathology, and treatment.

Beri-beri may be briefly defined as a non febrile disease, endemic, and limited to certain localities in which it may become epidemic; primarily manifesting itself through the nervous system by disturbances of sensation, motion, and cardiac and vascular control; including extensive serous effusion and localized muscular degeneration; often acute but exhibiting marked tendency to latency, chronicity and recurrence, and fatal in a considerable proportion of those attacked.

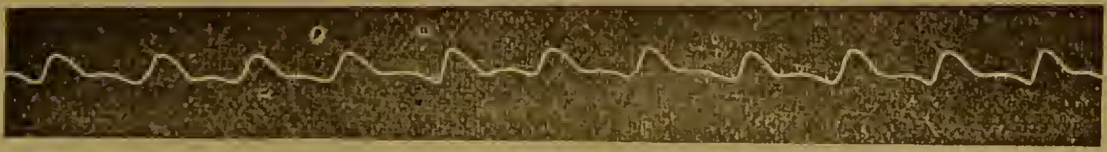
The cases seen divide themselves naturally and easily into three classes, acute, sub-acute, and chronic.

The acute form may appear without warning in a subject previously healthy, but as it far more often occurs in the course of a sub-acute or chronic case, it will be best described after the notice of such.

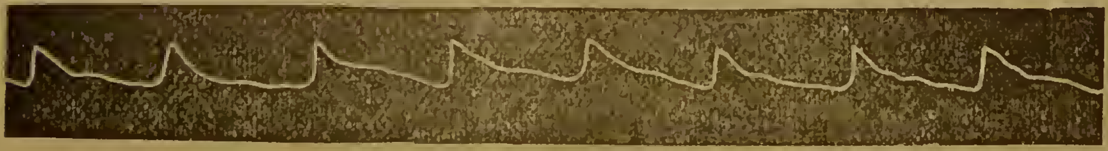
The sub-acute is the most usual form of the disease. The patient generally comes under observation complaining of a feeling of universal malaise, languor and muscular incompetency, which has possibly existed for some days or weeks. Examination shows that there is a clearly defined and unmistakable diminution or almost total loss of the sensibility of the skin upon the anterior surface of the legs below the knees, of the lower part of the abdomen, of the tips of the fingers, of the lips, or perhaps in all these situations. The shins and finger tips are the most common localities of this lesion. This anesthesia is, as a rule, clearly recognized by the patient, who calls the attention of the physician to its presence, but, in certain cases, even where other symptoms are well marked, may be so slight as to require the use of the esthesiometer for its detection. There is often also a loss of the muscular sense of the soles, so that the ground is not distinctly felt, a condition which, with some want of coördination generally present in these cases, determines a perceptible uncertainty of gait. Vague muscular pains are complained of, while deep pressure upon the muscles of affected parts, more particularly those of the calf and pectoral region, reveals the existence of much hyperesthesia of these organs. There is ordinarily, at this stage, some edema of the legs, which, when not excessive, is most distinct on the anterior surface from above the malleoli to the tibial tuberosity or a lower point. Severe palpitation of the heart is almost invariable, while many patients suffer from a sense of constriction about the base of the chest, a symptom which often causes severe distress. The pulse is one of high tension, as is easily detected by the finger and clearly shown in the sphygmographic tracings below, taken by the writer, using Marey's instrument at a medium pressure. This quality of the pulse is so well marked that one familiar with the disease will be led to suspect the nature of the case from the presence of this symptom alone. The heart's impulse is widely distributed, abnormal sounds are heard, suggesting valvular derangement, while both palpitation and auscultation detect at the cardiac base and for some little distance above that point, a peculiar semi-metalic, purring thrill, which, when clearly distinguished, is of itself sufficient to establish a strong presumption as to diagnosis. The appetite is fair, digestion usually good, though there is occasionally some irritability of the stomach, a symptom which should not be mistaken for the ill-omened emesis of the acute form, to be mentioned hereafter. The lungs are clear, the urinary secretion natural, the temperature normal or a little below normal; and, altogether, to an observer unacquainted with the possibilities of the case, there would probably appear to be little cause for immediate alarm. The experienced physician, however, knows well that, while the case before him will probably recover under prompt action, neglected it will drift into chronic disease, or even, should acute symptoms set in, that it may prove fatal in a few hours. In the beginning of my practice in Japan, nothing impressed me so much as the lightning-like rapidity with which just such cases as are described above would take on a condition in which treatment was hopeless and death to be anticipated at any moment.



SEVERE CASE SUB-ACUTE BERI-BERI.



AVERAGE CASE CHRONIC BERI-BERI.



RECOVERY FROM SUB-ACUTE BERI-BERI.

Should acute symptoms set in they generally do so without premonition. The heart's action becomes exceedingly rapid, the vessels of the neck pulsate violently, while the neck itself perceptibly increases in size from the intense congestion of which it is the subject; effusion into the peritoneum, pleura, or pericardium is rapid and often in large quantity, anasarca increases, dyspnea becomes intense, the complexion is livid, the distress of the patient is great and evident, frequent and painless vomiting takes place, the temperature rapidly sinks even below 90°, and, with but few exceptions death quickly closes the scene. The group of symptoms just described constitute the condition known to the native Japanese doctor as Shiyōshin, which he believes to be inevitably fatal. It is indeed but seldom that even the most prompt and enlightened treatmentis of avail in a severe case of this type; much depends upon the duration of the attack, which may be of but an hour or two, but is, more frequently, from twelve to twenty-four hours.

Chronic Beri-beri presents more or less of the symptoms of the sub-acute form. The pulse continues high in tension, various abnormal and often puzzling heart sounds are heard; the localized anesthesia and muscular hyperesthesia remain to a greater or less degree, the latter being most persistent and severe; the muscles of the extremities, especially those of the legs, degenerate and atrophy, cramps are not uncommon, while atrophic contraction of the muscles of the calf and leg induces marked deformity, and a peculiar gait which is almost pathognomonic. Exacerbations ofteu occur, short of the grave condition described above as the acute form of the disease; and the patient, if unrelieved by treatment, after months or even years of suffering from weakness, palpitation of the heart and muscular pains, may die from exhaustion, or extension of the paralysis to vital organs.

Such, briefly, are the prominent symptoms of Beri-beri as met with in Japan. In some cases there is undoubtedly anemia, but this is but a complication of the disease, and certainly does not constitute the chief, or even an important factor of the case, as was so long maintained. When death occurs it appears to be due, sometimes to failure of the heart, often to edema of the lungs, and, in some cases to pericardial or pleural effusion acting mechanically. Extensive effusion into the serous cavities is certainly more common in the northern part of the Empire than in Yedo or Yokohama, while, on the other hand, cases in which the purely nervous symptoms predominate are more frequent in the last named localities. There is always, however, a strong tendency to serous effusion, as may be demonstrated by the use of the ophthalmoscope, the fundus having appeared edematous in every case examined by the writer, irrespective of any perceptible effusion elsewhere, and in the earliest stage of the malady. Cases intermediate in character between the forms above described are constantly met with. In some, the paralytic and hyperesthetic symptoms may alone be present, in others dropsical effusions may at first glance seem to constitute the whole disease; again, a trifling and strictly localized edema, together with the slightest perceptible diminution of sensation over some very limited tract, may be the sole indications upon which to base a diagnosis, and so on in infinite variety. As a rule, the disease appears in the later summer and early autumn, though isolated cases occur at any time of year. The weather has a marked influence on the manifestation of the disease, at least within the season during which it is most prevalent. A day or two of wet, close and sultry weather is almost invariably followed by a large increase of the number of cases, as in 1878, when, in Yokohama, some fifty members of the police force were attacked within forty-eight hours, together with a large but unknown number in civil life.

Beri-beri is uncommon at the extremes of life, being most frequent after maturity and before middle age. Males suffer to a far greater extent than females, though the latter often succumb to the disease after childbirth, as in Hakodaté, where Beri-beri is the curse of the parturient woman No rank in society is entirely exempt, though the greater number of cases is encountered in the mercantile and student classes, and among soldiers and sailors. As compared with those of the occupationr just mentioned, the hard working and weather beaten farmer and coolie are but rarely attacked.

The sequelæ of Beri-beri require much more attention than has as yet been bestowed upon them. I am convinced that in many cases neither recurrent, nor of any long chronicity, the heart remains permanently affected, though not often to such an extent as to manifest its condition by the severer symptoms of cardiac disease. Anderson speaks of murmurs like those of organic heart disease, as being very common among the Japanese, during temporary and trifling disorders of health. I have noticed this fact, but in view of the great prevalence of Beri-beri in those parts of the Empire open to the observation of foreign physicians, am inclined to think that most of these cases may be traced to preceding attacks of Beri-beri, perhaps so slight as to have escaped observation at the time. Muscular atrophy has been noticed already in connection with the symptomatology of the milder forms. This, as well as localized indurations of the muscles, often persists as a sequel of the disease, and requires special treatment.

Etiology.—Beri-beri has been ascribed by different authors to malaria (Swaving, Lindmann), scorbutus (Praeger, Hellemann, Morehead), rheumatism (Dammann, Raile, Bernhardt), rapid and great alternations of temperature (Bontius, van Leent, Pruner Bey, Moens), anemia, and causes predisposing to anemia, as bad or insufficient food, overcrowding, faulty ventilation and the indirect effects of malarial influences (Reiche, Aitken, Christie, Rogers, Le Roy de Mericourt). Of the above named authors, Swaving, who considers the disease due to a progressive paralysis of the spinal cord produced by malaria ; and Lindmann, who ascribes it to spinal dropsy, the effect of paludal poison, appear to have more nearly touched upon the true pathology of the disease, in recognizing the important part played by the spinal-nervous system. Carsten also, in stating that Beri-beri, caused by a "certain morbid change of the blood," manifests itself by disturbance of the functions of the spinal cord, seems to have grasped this leading fact.

The phenomena of Beri-beri, as observed in Japan, bear a close resemblance in nany points to the known facts in regard to malarial disease the world over, while differing sufficiently to prove that the causes of the two diseases, however analogous in some respects, are essentially distinct.

Like malarial disease, Beri-beri has but a limited range, even in the regions where it is best known, and its localities are often sharply defined. In certain districts, generally, but not invariably, lying low and near the sea coast the disease is rarely absent, while within these districts there appear to be foci at which the cause of the malady manifests itself with greatest intensity. In other, perhaps closely neighboring, localities, generally inland and of higher level, Beri-beri never originates de novo, while removal to these districts affords by far the most certain and speedy means of recovering from the disease contracted elsewhere, as will be seen later. Again, newcomers to a Beri-beri district are infinitely more susceptible to the cause of the disease than are residents, susceptibility, other things being equal, decreasing pari passu with length of residence. On the other hand, the prevalence of Beri-beri by no means corresponds with that of malarial diseases, such as ague and remittent fever, either in time or locality, while Beri-beri is in no sense a febrile disease and, though recurrent, shows no periodicity. Quinine exerts absolutely no influence for good, other than as a tonic, in cases of Beri-beri, although, as is generally recognized, its action affords the surest means of diagnosis in malarial disease of obscure character.

Anemia, properly so called, rarely exists in Beri-beri save as an accidental complication. In cases of the dropsical variety (wet Beri-beri) the color of the skin, due to serous infiltration, the fluid being often a distinctly yellow color, has deceived many observers, while the undoubted power of deficient nutrition, exposure, bad ventilation, faulty drainage and other errors of hygiene, as predisposing causes, has induced others to seek in these the prime factors of the malady. The truth appears to be that Beri-beri is due to a specific poison, probably of telluric origin, the diffusion of which is much influenced by atmospheric conditions, and which, confined as a rule to certain localities, is capable of being transported, in some manner unknown, to regions heretofore unvisited, where, should it find the necessary conditions for prolonged existence and development, it may become endemic. In this connection it may be mentioned that at Hakodaté, where Beri-beri is now very prevalent and fatal, the disease appears to have been unknown until within a very recent period, though recognized in the more southern parts of the Empire for centuries.

Any cause which depresses the vital power, such as those noted above, or which specially predisposes to the contraction of disease in general, as childbirth, may determine an attack of Beri-beri, where the specific poison is present, but then only.

Beri-beri may be complicated by other diseases, as malarial and typhoid fevers. During 1877–8 a considerable number of cases of such complication were met with in Yokohama and puzzled us exceedingly at their first appearance. When malarial fever constitutes an element of the attack, this factor, with the symptoms dependent upon it, is quickly eliminated by the administration of quinine. Cases complicated by typhoid are naturally more unmanageable, present a mixture of the symptoms of the two diseases but slightly modified, and probably have a much higher rate of mortality than either of the component diseases alone.

SUSCEPTIBILITY TO AND PERIOD OF INCUBATION OF THE DISEASE.

The question of personal susceptibility has been to some extent, and incidentally, dealt with above. Many persons appear to enjoy entire immunity. Anderson considers a residence of six or seven months, within an infected district, requisite to determine an attack, which may appear after removal to a region where the disease is uncommon or unknown. This however is rare. I am inclined to believe that in exceptional cases a much shorter exposure may suffice. The author just cited, who was connected with the Japanese naval service, mentions as an instance of the appearance of the disease, after removal from its usual habitat, the case of the Japanese man-of-war Tsuyuba Kan, in which the men were attacked at the rate of two or three per week during the voyage from Yokohama to San Francisco and returning, one fatal case occurring just before arrival at the home port, six months after departure therefrom. In this voyage there is reason to believe that many of the predisposing causes were combined to an extent sufficient to neutralize the favorable influence of removal from the infecting locality.

The tendency of the disease to become chronic, and to become latent for long periods, must be considered in this connection.

Slight attacks are often unrecognized, and what is believed to be the first manifestation of the malady, may really be a recurrence.

If I read aright the history of the outbreak on the Brazilian corvette Vital d' Olivera, as outlined in the PACIFIC MEDICAL AND SURGICAL JOURNAL for September last, the cases appearing on the voyage up to Hong Kong were recurrent, chronic or delayed: while a new supply of Beri-beri poison was received by the crew at Yokohama, a favorite habitat of the disease, competent both to cause further recurrence and to originate new cases. It will be noticed that the weather, while the ship remained in Yokohama, was specially favorable to infection, and that many of the causes most strongly predisposing to attack were in operation throughout the voyage.

FREQUENCY AND MORTALITY.

Statistics are everywhere wanting as to the frequency of occurrence of the disease, in the population at large. Returns of the Japanese military forces at various posts within districts subject to Beri-beri, for 1875, which is taken as a fairly average year in this respect, indicate an occurrence of cases in the ratio of from 26 to 33 per cent. of those exposed, including cases of all degrees of severity. It must be remembered, however, that the soldiers furnishing this enormous proportion of cases were, almost without exception, new arrivals in Beri-beri districts, and from this fact alone strongly predisposed to attack.

The mortality of the disease, as regards the total number of cases of all classes, it is equally impossible to state, even approximately. Various authors have given the fatality in India as from 15 to 33 per cent of those attacked. Da Silva Lima of Brazil, in his earlier papers, estimates it as high as 50 per cent. after all possible deductions; later it is given as 25 per cent. Anderson gives the death rate of army cases in Japan, during 1875, at 17.6 per cent., the range for different stations varying from 13 to 30 per cent. The greatest mortality was at the northern stations, a fact which, taken with that of the prevalence of the disease at Hakodaté, lat. 41° 45″, forbids us longer to consider that Beri-beri is exclusively a disease of tropical, or even sub-tropical climates. My own experience of practice in civil life among the Japanese would indicate a much lower rate of mortality than is shown by the foregoing statistics. With the exception of parturient women, in whom the disease was apparently inevitably fatal, I should say that about 10 per cent. of all cases within my knowledge have resulted in death. A large number of my cases, however, have been of recurrence, or very mild; and as I have for some years insisted upon immediate removal beyond the district where the disease was prevalent, as the first point in treatment, my estimate will, in all probability, fall far below the true one for cases otherwise treated.

The almost entire exemption of foreigners in Japan is a singular fact in the history of the disease. So far there is not a single well authenticated case of any one of European or American blood having suffered from its attack. This may be due to the circumstance that few foreigners are subjected to any of the strongly predisposing causes. Most European and American residents live with exceptional comfort, while the sailors waiting shipment, probably the only class of foreigners, with one exception, subjected to bad hygienic influences, as a rule, remain but a very short time, in all probability not long enough for that saturation with the poison which seems necessary to the production of the disease. The exception mentioned is that of the considerable Chinese population. These, in Japan, as elsewhere, live in utter violation of decency and cleanliness, and, perhaps from this fact, suffer occasionally from Beri-beri, though certainly not to the extent that would be expected. Remembering that in other countries natives of almost all the European countries have suffered, and suffered severely, from Beri-beri, we have no right to assume that there is any exemption on account of race; while the known range of the disease from 42° north to 25° south latitude, and in both hemispheres, forbids any idea of geographical, or perhaps even climatic, limitation of an absolute character.

DIAGNOSIS.

The diagnosis of Beri-beri should present little difficulty in well marked cases. The pathognomonic symptoms are generally to be found if sought for, chief among these being the combination of deep hyperesthesia with superficial loss of sensation. It is quite conceivable, however, that upon the first appearance of the disease in any locality, cases in which those symptoms are but slightly developed and the complaints of the patient are of malaise, constriction of the chest and irregular action of the heart, the physician may be misled, especially in view of the general presence of anomalous heart sounds and the frequent existence of edema. The edema of Beri-beri has, however, certain peculiarities in its distribution, elsewhere noted, which alone would serve to arouse suspicion as to the nature of the case, in one of experience.

Careful examination will nevertheless reveal some of the peculiar features of the disease, even in the most obscure cases, while the history of exposure within a Beri-beri district will establish the diagnosis beyond a doubt.

Post-mortem appearance.—Many more and much fuller investigations of the conditions after death than have yet been made are exceedingly to be desired. Accounts of autopsies in India and the Malay Archipelago are neither numerous nor complete, and are often perceptibly biased by the preconceived ideas of those reporting them. But few opportunities for post-mortem examination have as yet been been obtained in Japan—I believe but five in all, so far as foreign physicians are concerned. However thorough may have been the work performed in these few instances, it is much to be regretted that the government of Japan, so enlightened and progressive in some respects, does not avail itself of the abilities of some of the thoroughly competent foreigners in its service, by at the least granting them necessary facilities for an investigation which would be eagerly undertaken and could scarcely fail to prove of immense benefit to the nation. It is solely to the voluntary labors of foreign medical men resident in the country, pursued under most discouraging circumstances, that is due the discovery and demonstration of the importance of the removal of cases of Beri-beri beyond the district of the prevalence of the disease, a discovery which already saves annually an immense number of valuable lives.

In cases where the dropsical symptoms have been prominent, the cellular tissue is found more or less infiltrated, sometimes to an enormous extent. This edema may include the entire body, with the singular exception of the posterior aspect of the trunk, which I beieve is never invaded. The condition of the muscular system varies according to the stage of the disease at which death takes place. In acute dropsical cases the muscles may be well developed and to all appearance normal. In cases where death is preceded by long suffering and the various nervous disturbances described under symptomatology, more or less localized atrophy of the muscles exists.

The serous cavities contain a greater or less amount of fluid, the pleuræ and pericardium being most frequently and seriously affected, the peritoneal cavity least so.

The lungs are sometimes edematous or collapsed under the pressure of fluid, occasionally deeply congested and again almost normal.

The right heart and whole venous system are gorged with blood, the left heart sometimes containing blood, sometimes empty or showing acute ante-mortem coagulation. The heart is flabby, sometimes dilated and hypertrophied, its tissue softened, though as a rule exhibiting no specific degeneration, while the closest scrutiny reveals no cause for the valve-like murmurs so generally present before death.

The liver is congested, edematous or normal, rarely enlarged; the spleen, which is seldom perceptibly enlarged during life, is generally congested and softened. The intestines are as a rule congested and injected, sometimes to a remarkable degree. Anderson found denudation of the intestinal epithelium, with ecchymoses. The kidneys have generally been found healthy, though some authors speak of fatty degeneration and other lesions similar to those of the various forms of Bright's disease. Considering the excessive rarity of albuminous or other evidence of disease of these organs during life, such conditions of the kidneys are probably exceptional.

The cerebral meninges are more or less congested and infiltrated. The brain substance has been considered normal, or at most edematous. The cerebral capillaries were thought by Anderson, in his solitary autopsy, to bear evidence of prior distension, though empty when examined; a condition which he found to obtain in the spinal cord also.

The spinal canal, where examined, has contained a large excess of fluid. The meninges of the cord are congested, and in one case at least are said to have exhibited extravasations. The cord itself has, with few exceptions, been found softened in some part of its length, the lower portion being least affected. Some authors claim to have detected large numbers of corpora amylacea in the medullary parenchyma. Magathaes, in the PACIFIC MEDICAL AND SURGICAL JOURNAL for September, 1880, speaks of having encountered spots o- ecchymosis at the emergence of the nerve roots, a condition which If do not find noticed elsewhere.

The autopsies which have been obtained by foreign physicians in Japan have not only been secured with difficulty, but often performed under circumstances rendering a thorough or satisfactory examination impossible.

The conditions in the body examined by myself were briefly as follows:

The subject was a prisoner in the jail at Hakodaté, and succumbed to the acute dropsical form of the disease, the immediate cause of death appearing to have been pericardial effusion. This was one of the first cases of Beri-beri which came under my observation.

Anasarca, general save in dorsal and lumbar regions; muscles well developed and of good color; skin much ecchymosed.

Cranium—Meninges much congested, blood very fluid, a condition afterward found to prevail throughout. Slight effusion of yellow serum beneath membranes. Cerebral parenchyma edematous, ventricles contain an abnormal amount of yellow serum.

Spinal Canal and Cord—Much deep yellow fluid through whole length of canal, cord and its membranes apparently normal, save in lumbar region, where the membranes were intensely congested and the cord itself enlarged and so softened as to make its removal a matter of difficulty.

Thorax—Much deep yellow serum in both pleuræ, no adhesions, left lung solidified by pressure, due both to the pleural effusion and to that in the pericardium, the latter containing some two quarts of the generally present yellow serum. Heart enlarged, dilated and hypertrophied, ante-mortem clot in left ventricle, right heart and venous system generally enormously distended with fluid blood, muscular tissue of heart soft.

Abdomen.—Some two or three quarts of yellow serum present. Liver enlarged to nearly double usual size, pale and marbled in section. Gall bladder, stomach, intestines, pancreas and kidneys apparently normal, spleen enlarged and softened.

Microscopic examination of the softened portion of the cord showed great distension of the capillaries with many small extravasations. The heart tissue was fatty, as was that of the liver.

It will be observed that the liver was found much diseased in this case. It is impossible to say to what circumstances, independent of the attack of Beri-beri this may have been due, as I could obtain no history of the case antedating the final illness. The disease of the liver was, in all probability, the cause of the deep staining of the effused fluid noted as above.

Treatment.—No remedy exercising specific action on Beri-beri has yet been found. Quinine, the sulphites and chlorides, carbolic acid, and other supposed anti-zymotics have been faithfully tried, the first extensively, owing to the belief of some that the disease is due to malaria. Da Silva Lima has faith in arsenic, but as he reports perhaps a larger mortality than any other observer, his faith seems misplaced. In the hands of others, myself among the number, it has failed to produce any beneficial effect.

No specific being known, the treatment must necessarily vary with the symptoms. In the dropsical form, long experience, here as elsewhere, has demonstrated the value of depletion by purgatives and diuretics, the former being by far the most efficient. The salines are most useful in the majority of cases of subacute and chronic form. In the acute form, where effusion is going on with great rapidity, more active and drastic purgatives are required. In this stage, Anderson, following Marshall, Patterson and Hamilton, recommends large and repeated bleedings, and, in desperate cases, where the bowels fail to respond to cathartics, as they often do, and the weakened right heart is clogged with the blood, suggests the propriety of aspirating the heart itself. Aspiration of the pericardium has been practiced in a few cases but I believe without ultimate success. In the single operation of this nature performed by myself, relief, though temporary, was great and immediate, and I shall not hesitate to repeat it under similar circumstances. The supply of fluids should be limited and the functions of the skin stimulated, while measures should be taken to maintain the warmth of the body. Stimulants, both alcoholic and aromatic, have been recommended by many authorities in all stages of the malady. In my experience I have seen little good result from their administration.

As regards the milder types of the disease, paresis may be combated by strychnia, electricity and massage. The general experience seems to be that when muscular hyperesthesia is combined with the paresis the two former are injurious. No remedy is so efficient for the reduction of this hyperesthesia as aconite. I am informed by Dr. Simmons of Yokohama, a physician whose experience in the treatment of Beri-beri has been exceptional, and who is now preparing a monograph on the subject, that aconite has long been used by the native profession for this purpose, and that his personal experience of it has been favorable. I have of late used it to a considerable extent and have found it beneficial in rather more than half the cases in which it was given. Phosphorus has been suggested, and Anderson speaks highly of it in cases of localized atrophy following the more acute forms. In view of the well known effect of this remedy in producing degeneration of the cardiac tissue, it should be handled with care in a disease of which an important element is weakening, possibly degeneration of the heart. The same remark will apply to Jaborandi, which would suggest itself as a valuable depletory, if only the tendency to effusion be considered. In one case, in which I administered this drug, almost fatal collapse followed, apparently from its depressing effect on the heart. Digitalis, while it is most useful in mild, seems powerless in severe cases either as a cardiac stimulant or as a diuretic. Diuretics, as a rule are far less to be depended upon than carthartics. Although the kidneys are almost invariably healthy, as noted above, it seems exceedingly difficult to stimulate them to increased action. Ergot, veratria and nitrate of silver are recommended by Dammann; the former at least would seem to deserve a trial. Tonics will often be required, and the diet under all circumstances should be light and highly nutritious. The experience of native physicians has led them to interdict the use of rice as the first step in treatment. For this they sometimes substitute other cereals, but more often a small red bean, which of itself possesses some diuretic power.

But all treatment of a medicinal nature will frequently prove useess or inefficient even in mild cases, which, it must be remembered, in this disease, more than most others, may at any moment assume most alarming severity, so long as the patient remains within the range of influence of the cause of the disease. Prompt removal if it can at all supported, is the first thing to be insisted upon, to a higher lying country if possible, and away from the coast, but at least to a region in which no cases have been known to originate. It is by no means always requisite that the patient should travel to any great distance. In some localities a perfect sanitarium, so far as Beri-beri is concerned, may be found within five miles of the point of infection. This is the case in Hakodaté, and, I think, in Yokohama also, though at the latter place, as a rule, we prefer to order patients to the mountains, a distance of thirty to forty miles, believing that, in addition to escape from the influence of the specific poison, we thus secure the usual advantage of complete change of air and surroundings.

The importance of change of residence in the treatment of Beri-beri is rapidly becoming known to the people, and it seems not unlikely that the government may soon be induced to establish sanitariums or hospitals at proper locations, the value of which would be beyond computation.

The rapidity with which many cases of Beri-beri recover, after removal to a healthful locality, is sometimes almost miraculous, as is, unfortunately, the equal rapidity with which the disease often asserts itself upon the return of the patient within the sphere of its action.

The foreign physicians here await with much interest the results of the observations on the cases of Beri-beri which have fallen into the hands of the San Francisco profession, as the obstacles which have so seriously interfered with the study of the disease in Japan are not likely to hamper investigation on the other side of the Pacific.

NOTE—In reviewing the earlier portion of this paper I find that I have stated absolutely and without modification that the state of the arteries is that of tension. This is undoubtedly true as regards most cases of the disease in its earlier and least severe stages. In the acute and imminently dangerous form, the opposite condition obtains and the phenomena are those of vasomotor paralysis. I cannot at present lay hand on the sphygmographic tracings illustrating this fact, but the appearances both before and after death indicate clearly that such is the case.

P. 10885
6

J. GRATEROL Y MORLES

CONTRIBUCION
AL
ESTUDIO DEL BERIBERI

CARACAS
Tipografía Americana
1930

CONTRIBUCION AL ESTUDIO DEL BERIBERI

El autor del trabajo de este título, enviado a la Academia Venezolana de Medicina y pasado reglamentariamente al examen e informe de la Comisión de Patología Médica, que me honro en presidir, comienza estableciendo que «si la existencia de una avitaminosis (en este mal) está fuera de duda como causa del Beriberi, hay muchos casos en que es forzoso invocar la acción de otros factores etiológicos».

La Comisión, y muy particularmente el que suscribe, está perfectamente de acuerdo con aquel postulado. «El Beriberi es una forma de neuritis periférica múltiple, que ocurre endémica o epidémicamente», es la definición de un tratadista del día, con la cual concuerdan todos, y en todos mis artículos y lecciones sobre la materia he sostenido que, por lo menos en Venezuela, no está en la alimentación la causa principal del Beriberi, pues se le ha visto aparecer y desaparecer en varias regiones del país, sin que el régimen alimenticio haya cambiado en lo más mínimo, y que por tanto, hay en su etiología un elemento infeccioso, pues la manera de presentarse y de propagarse ha sido la de toda infección y hasta se han referido casos numerosos de contagio indudable. El hecho de no haberse señalado hasta ahora un microbio específico no es un argumento en contra. Son tantas las infecciones de germen desconocido!

Ni aún el Bacilo del *Kaké* de los observadores brasileros, ni el *Bacilus astherogenes* del Comité de la Indochina, a los cuales dedica varios párrafos el autor del trabajo en referencia, han tomado posesión de un puesto indiscutible en el cuadro de la etiología infecciosa microbiana. El niega también, y con razón sobrada, el origen palúdico del Beriberi.

En seguida detiénese el autor en describir un caso clínico de su clientela, en que las manifestaciones neurales llegaron a invadir la médula, hasta terminar por la muerte, y compara este caso de parálisis por *infección* con otro también de su clientela, de parálisis *por sección medular*, apoyándose en ellos para concluir que las lesiones ánatómicas del Beriberi no son solamente de los cordones nerviosos, sino también de los cordones medulares y justificar así la proposición que hace de llamar este mal *polineuromielitis toxinfecciosa*, en la cual denominación van comprendidas la lesión y la causa.

Es de notar que los autores más antiguos y los más modernos señalan en el Beriberi lesiones de los centros nerviosos, al lado de las localizadas en los cordones neurales, lo cual no impide que se siga considerando, como lesión principal en el Beriberi, la polineuritis. sin perjuicio de extenderse hasta los centros meningo-cerebro-medulares. Sin embargo, se sigue designando la enfermedad con el nombre de *neuritis*, acaso por brevedad, sin que el hecho indicado amerite un cambio de denominación, innecesaria, si bien justificada.

Encuentra el autor inexplicable en el Beriberi «ese confinamiento del proceso morboso a las porciones dorsal y lumbar de la médula, cuando la infección ha debido invadir todo el sistema nervioso.. » «y lo atribuye a un factor oculto, cuya esencia ignoramos».

No es este un hecho insólito. Todas las infecciones tienen sus localizaciones que no siempre se limitan, sino que se extienden en el mismo o en diferentes aparatos, y no es por tanto digno de admirar que si el Beriberi se localiza principalmente y a veces sólo en los cordones nerviosos, otras se propaga a las meninges, al cerebro y a la médula, pero que siendo la más constante y característica de todas, aún en las formas más benignas, las neurales, se haya llamado y se siga llamando la enfermedad *neuritis* o *polineuritis*, como se llama poliomelitis la parálisis epidémica que interesa también el encéfalo, o *dotinentería*, la fiebre de tan extensos alcances anatómicos.

Salvo estas breves observaciones, la Comisión aplaude el esfuerzo representado por el interesante trabajo del Dr. Graterol y Morles, que ojalá tuviese imitadores.

En la conclusión, la Comisión opina:

1—que el Beriberi no es exclusivamente una avitaminosis, sino que en su etiología hay un elemeto infeccioso desconocido hasta ahora, en lo cual concuerda con el autor del trabajo examinado:

2—que el hecho de extenderse hasta la médula las lesiones neurales del Beriberi, que son las principales, no amerita un cambio de nombre, diciendo, en vez de *polineuritis*, como generalmente se dice, *polineuromielitis*, como propone el autor del trabajo.

Por la Comisión.

El Presidente,

Francisco A. Rísquez.

CONTRIBUCION AL ESTUDIO DEL BERIBERI

PARA LA ACADEMIA DE MEDICINA.

A mi honorable amigo y colega Dr. J. Sanabria Bruzual.

Descripción de un caso insólito que da margen a emitir algunos postulados de Fisiopatología nerviosa y que nos lleva a pensar que en esta afección, las lesiones no están limitadas a solo los nervios periféricos, sino que se propagan hasta la médula.

No es mi propósito presentar aquí una monografía acabada sobre el Beriberi. Concienzudos trabajos se han publicado sobre tan importante asunto; pero aun queda vasto campo inexplorado a la investigación científica. Reina gran oscuridad sobre puntos esenciales de la historia de esta entidad morbosa. Se discute sobre su naturaleza, y a este respecto ninguna teoría exclusivista satisface las exigencias de la Clínica. Está probada la influencia preventiva de ciertas sustancias, llamadas vitaminas; defensas naturales que el organismo encuentra formadas de un todo en algunos alimentos, las cuales al fallar por algún tiempo en la alimentación diaria, originan trastornos en el metabolismo normal. Así se producen las enfermedades llamadas por carencia: se explica la aparición del escorbuto en los largos viajes trasoceánicos, como la génesis en otras circunstancias especiales, de la pelagra; o el desarrollo del latirismo en casos más particularmente excepcionales. De igual modo el beriberi, síndrome neurodegenerativo, sería causado por la avitaminosis «B», o sea por la ausencia en la alimentación de la vitamina de Funk, nombre de su descubridor y quien estudió primero sus propiedades. La existencia de esta avitaminosis está fuera de toda duda y principalmente comprobada en los pueblos asiáticos, con verdadero acopio de hechos, observaciones clínicas y experiencias de laboratorio; pero hay muchos casos de beriberi en que es forzoso invocar la acción de otros factores etiológicos. Aunque los autores de ultramar niegan rotundamente la contagiosidad de esta afección, aquí, en Venezuela, y particularmente en la región guayanesa, donde es endémica, se han podido constatar casos de contagio, por lo menos mediato o por infección, en una sala de hospital y en repetidas ocasiones; y esto no se compadece absolutamente con la teoría exclusivista de la deficiencia alimenticia, Además, abundan las observaciones en que se ha visto sobrevenir el beriberi fuera de todo régimen de carencia. Puede en ciertas circunstancias figurar la avitaminosis como causa predisponente, cuyo aporte sería el de preparar el terreno al enemigo, privando al organismo de una defensa natural.

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Así como en la difteria, la lepra, la escarlatina y el tétanos, los microbios de estas enfermedades elaboran toxinas que van a intoxicar los elementos nerviosos y producir en consecuencia neuritis diferenciadas; nada tiene de aventurado, y sí mucho de lógico, el suponer que suceda lo mismo en la patogenia del beriberi. Y si aquellas toxinas afectan las neuronas en toda su extensión, desde el cilindroeje de los nervios periféricos hasta las células motrices de los cuernos anteriores, es racional creer que en el beriberi se desarrollen análogos procesos. El beriberi es en efecto, una enfermedad infecciosa acompañada de toxemia.

No es ya una mera suposición, sino un hecho averiguado, que la infección se propaga por los *vasanervorum* al través de las ramas y troncos nerviosos hasta los segmentos correspondientes de la médula.

Claude en un caso particular de intoxicación experimental, prolongada y repetida por la toxina diftérica ha observado, al lado de fenómenos paralíticos, trastornos tróficos; y en la autopsia del animal, lesiones neuríticas de los cordones posteriores y del cordón de Goll. Iguales alteraciones han producido experimentalmente Henríquez, Crock, Mourawieff y Mouratof.

Hay un trabajo muy importante del Dr. D' Hamilton Wright, Director del laboratorio especíalmente instalado para hacer el estudio metódico del beriberi en los Estados Malayos. En él este histólogo dice que ha podido constatar en muchos de los casos que se presentan allá con bastante frecuencia, además de la neuritis, lesiones muy acusadas de las células ganglionares en la médula y en el bulbo. De sus investigaciones concluye por decir este autor: «que la neuritis beribérica no difiere radicalmente de las otras neuritis parenquimatosas y que según todas las probabilidades el trastorno funcional o la destrucción de las prolongaciones axiles, resulta del trastorno o de la destrucción de los centros tróficos». A lo cual agrega Jeanselme: «parece que en el beriberi, como en muchas otras afecciones, se ha cometido el error de localizar *demasiado estrechamente* la lesión en las expansiones periféricas. «Es verdad que la neuritis es la expresión más frecuente de esta enfermedad, pero es también muy probable que el veneno beribérico, afecte, según los casos, todo el sistema nervioso,

¿En qué orden se desarrollan estas lesiones? «Los hechos experimentales tienden a probar que las lesiones de mielitis son las primeras que puede apreciar el histólogo. Lo que no quiere decir que la fibra nerviosa no estuviese ya interesada, sino que su degeneración no es reconocible desde un principio al microscopio». (Claude)

Ya Le Dantec decía en su Patología Exótica, 1ª edición, al abordar la anatomía patológica del beriberi. «Se han practicado pocos exámenes microscópicos del eje nervioso espinal; la médula está algunas veces reblandecida al nivel de sus dos expansiones y en su tercio inferior». «Los autores brasileños han observado la presencia de manchas equimóticas. De Baels ha visto las células de los cuernos anteriores degeneradas y una infiltración embrionaria al rededor del ependimo». Creemos pues, que la médula es invadida *d'emblée* junto con los pares fisiológicos que emanan de los segmentos infectados.

Los Dres. Grall y Clarac en su Patología Exótica de 1926 decían: «Nuestra actual incertidumbre no puede ser un argumento decisivo contra la teoría infecciosa del beriberi; muchas enfermedades son incuestionablemente consideradas como infecciosas sin que su agente patógeno sea conocido. El beriberi tiene el aspecto, la marcha, los sobresaltos epidémicos de las enfermedades infecciosas: solo el origen microbiano es capaz de suministrar una explicación satisfactoria de los hechos observados; nuestra ignorancia sobre un agente patógeno indiscutible, no debe ser sino motivo de incitación para ulteriores investigaciones, no una razón de negación».

El presentimiento que palpita en estas frases, parece ya cercano a una realidad tangible. Dos series paralelas de investigaciones clínicas en colaboración con el laboratorio han sido emprendidas en dos regiones distintas con resultados halagadores y casi definitivos, en el Brasil y en la Indochina.

Tomamos del Boletín de la Oficina Pan-Americana, correspondiente al mes de octubre en curso, lo siguiente:

«En el Brasil los autores han verificado una alteración en la flora intestinal de los animales en experiencia, los cuales, bajo este punto de vista, se distinguían completamente de los individuos normales. Han encontrado en los animales atacados de polineuritis gallinarum un bacilus que aparece en las heces, como una muestra de cultivo, casi pura. El germen en cuestión no aparece en el tubo digestivo de los animales sanos, sino exclusivamente en los animales beribéricos. Se le ha dado el nombre de bacilo del *kaké* (denominación regional del beriberi en el Brasil). Este microorganismo presenta todas las características de los bacilos del grupo *coli.* Es gram-negativo, móvil, desprovisto de espórulas y morfológicamente imposible de distinguir de la variedad común del bacilus *coli;* no licúa la gelatina, produce indol a partir de la peptona, coaugula la leche, crece en agar de modo característico. Difiere del bacilus *coli comune* (Escherich), por el hecho de producir ácido y gas en los medios que contienen sacarosa. De estos hechos vino la idea de que pudiera muy bien ser una forma anormal de desenvolvimiento del bacilo *coli communior* (Durhan); más, después de observar las reacciones específicas de inmuno-sero con este bacilo, púdose concluir que el B. *kaké* difiere completamente de los otros representantes del grupo colibacilo. El número de días que transcurren desde aquel en que la dieta deficiente es administrada hasta el en que aparece el bacilo *kaké* por primera vez en las heces, varía indefinidamente; en tanto que el lapso que media entre la aparición del bacilo específico y las primeras manifestaciones clínicas de la enfermedad, es más o menos fijo. En particular, sin excepción, todos los animales mostraban signos clínicos de polineuritis dentro de quince días después de la aparición del bacilo en las heces. De estos estudios resultó la convicción de que el período de incubación es hasta cierto punto acortado y uniformado cuando se da a los animales los cultivos del bacilo por vía oral. Parece también que el germen ingerido provoca activamente la dolencia en los animales experimentados. Más en todo caso, está probado que en esos animales el B. *kaké* aparecía en las heces desde algunos días antes de estallar los síntomas del beriberi. También durante el ataque se verificaba la presencia del germen incriminado de un modo casi constante. Cuando no se encontraba más el bacilo específico en las heces, o cuando empezaba a disminuir, era porque la infección beribérica iba marchando hacia la curación.

En el Hospital de la Universidad de Chiba y en el Hospital Militar de la misma ciudad, durante el verano pasado examináronse las heces de personas que nunca habían sufrido enfermedad que se pudiese catalogar como beriberi. También practicóse examen de las heces de más de 400 soldados que hacían parte del regimiento de Chiba. En todos estos casos el B. del *kaké* fué encontrado en la proporción de 1%. Como por el hecho de la presencia del bacilo específico en personas que nunca habían tenido beriberi surgía un detalle de la mayor importancia para la dilucidación de la cuestión etiológica, se procedió al examen basterioiógico de las heces de más de 100 habitantes en la ciudad de Narita, provincia de Chiba. Ese examen fué practicado durante los meses de diciembre de 1927 a enero de 1928. El resultado de estas pesquisas fué que, de 2103 personas cuyas heces fueron sembradas en placas, conteniendo el medio de sacarosa ácima, 101 estaban infectadas por gérmenes que producían coloración bermeja de la placa. Mas, de esos 101 personas, la mayoría lo que acusaba era el bacilo communior de Durhan, y por la aplicación del sero-diagnóstico diferencial, esta variedad era fácilmente distinguida del verdadero bacilo del *kaké*, el cual de hecho, sólo existía en 18 de las 2103 muestras de heces, lo que también representaba poco menos del 1% de los individuos examinados. La misma proporción que se observa por lo demás, en individuos sanos atacados de otras dolencias, que son portadores del bacilo del beriberi, y más o menos la misma que se encuentra en relación a la disentería y a la fiebre tifoidea.

Por lo que hace a la reacción de la aglutinación específica del B. del beriberi por la sangre de beribéricos, siempre se obtuvo con el suero de los enfermos tratados en la Universidad de Chiba. El título en que el suero de los beribéricos aglutinaba el bacilo específico varió de 1 para 200 a 1 para 500. El porcentaje de resultados positivos de la reacción de aglutinación del B. del *kaké* por el suero de 30 beribéricos fué de 83 con 3%. También hiciéronse reacciones de aglutinación del bacilo específico con suero de individuos normales y con el de enfermos que sufrían de otras dolencias. En la mayoría de los casos el título a que dicho suero aglutinaba el bacilo en cuestión era inferior al 1 por 50 y por consiguiente la reacción era negativa. Así pues, de la observación de los hechos resultantes del trabajo experimental, se deduec que el baci'us *kaké* debe ser la causa principal de la producción del beriberi experimental en los animales.

De un modo general se puede decir que la mayoría de los dolientes de beriberi, con la enfermedad ya confirmada, tienen o tuvieron en un corto período de tiempo el bacilo específico en las heces. En contraposición, no se encuentra el bacilo ni en las personas ni en los animales que están libres del beriberi. Cuando el bacilo es dado por la boca la infección ocurre y las manifestaciones de la dolencia no se hacen esperar. Tanto por el suero de las personas naturalmente atacadas de *kaké*, como por el de los animales enfermos artificialmente, el bacilus específico es aglutinado a un título elevado.

En otras palabras: el beriberi o *kaké* no es sinó una enfermedad infecciosa que solo ocurre cuando se produce la infección por el B. *kaké* identificado.

A iguales conclusiones han llegado los bacteriólogos que han investigado en el Oriente, en una región antípoda de la del Brasil.

Tomamos del Boletín de la misma Oficina Sanitaria Pan-Americana que se publica en Washington, correspondiente a julio del año pasado la siguiente información:

«En la sesión de noviembre de 1927 del Comité Permanente de la Oficina Internacional de Higiene Pública, L'Herminier recordó las investigaciones llevadas a cabo por el Dr. Bernard, Director de los Institutos Pasteur de Indochina, las cuales han conducido a las siguientes conclusiones: (a). Se ha aislado y cultivado el *Bacilus Astherogenes*, considerado como agente específico del beriberi; (b). Se ha reproducido experimentalmente la enfermedad en el animal; (c). Se ha verificado la reacción de desviación del complemento; (d). Se han hecho ensayos de vacunación satisfactorios».

Ante estos resultados tan impresionantes, obtenidos por investigadores que trabajan a tan largas distancias, y que coinciden en muchos puntos esenciales, creo que se ha penetrado ya en el mecanismo biológico de este complexo morboso: Faltaría solamente establecer la identidad biológica entre el *Bacilus Astherogenes* del sabio investigador de la Indochina; y el B. del *kaké*, de los autores brasileños.

Por lo que hace a la teoría que considera al beriberi como una modalidad del paludismo, como una de sus formas larvadas, carece desde luego, de todo fundamento científico. El paludismo no es una enfermedad exclusivamente tropical. En la Campiña Romana, en toda la zona que rodea a las lagunas Pontinas, como en otras regiones comprendidas en las zonas templadas, es endémico el paludismo; ¿cómo es que ha podido suceder que hasta la fecha se haya escapado a la sagacidad de clínicos tan eminentes como un Bachelli, un Borelli, &, &, la apreciación de este síndrome enteramente exótico allá; y que no figure el beriberi entre las formas perniciosas o larvadas del paludismo, que ellos han estudiado y descrito tan magistralmente en sus obras? Además, en los análisis citológicos que se han hecho dela sangre de enfermos beribéricos no se han encontrado plasmodios ni gametos, ni ninguna de las formas intermediarias, características del paludismo, que pudiera dar margen a semejante clasificación. No encaja el beriberi, con la complejidad de sus manifestaciones y con su insólita fisonomía, en ninguno de los moldes conocidos del paludismo. ¿Y, cómo es que, la terapéutica específica del paludismo, (quinina, arsénico, azul de metileno, &c)—no produce ningún beneficio en los beribéricos, como debiera suceder, si ambas enfermedades tuvieran el mismo origen?......

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Con tales consideraciones etiológicas y patogénicas, paso a hacer la exposición de un caso insólito, entre otros que tuve ocasión de observar en mi estada en Guayana, y cuyo síndrome clínico es de tal modo sugerente y se destaca con tan subido relieve, que sin desviarme del criterio convencional, creo que es necesario ensanchar un tanto el concepto nosológico de polineuritis, con que se viene calificando hasta hoy el beriberi. De tal modo se desprenden los grupos sintomáticos, tan localizados y circunscritos a los respectivos sistemas y aparatos, que, por lo menos para casos de la índole del que ahora nos ocupa, hace falta una denominación más propia, más amplia y ajustada a los hechos. Yo me atrevería a proponer el término de *polineuromielitis toxinfecciosa*.

He aquí el caso: joven de 31 años, sano, vigoroso y bien conformado, sin ninguna tara hereditaria; tenía ya 20 meses de residencia fija en Paruruvaca (Alto Cuyuní); empieza a sentir adormecimiento en las piernas, el cual se va acentuando hasta obligarlo a trasladarse a Tumeremo, lugar en donde el suscrito estaba a la sazón ejerciendo en 1918. Principié el examen por los conmemorativos: me habló de su estada en la mina de Corocoro, donde tenía ya cerca de dos años de permanencia fija. En este retiro reina endémicamente el beriberi, y es fama que son muy contados los que escapan de contraer el mal, pasados los primeros seis meses. Como a este joven me ligaban antecedentes (era hijo de un antiguo amigo mío), fuí a encontrarlo en auto al sitio de la Manga, hasta donde pudo venir, haciendo grandes esfuerzos, a caballo. Al subir al vehículo hube de advertir la impotencia de sus piernas y tuve que ayudarlo, y más difícil le fué descender cuando llegamos al hotel. Todavía esa tarde pudo ir, llevado del brazo, al comedor, lo que no pudo efectuar ya, al día siguiente. Inquirí sobre su régimen alimenticio; contestóme que era el ordinario de esos lugares: legumbres, verduras, plátanos, carne, casi siempre salada, y con más frecuencia arroz, papelón (azúcar no refinada) y casabe. Le hice hincapié sobre la calidad y condición del arroz: si era del muy blanco y pulido que importan del exterior, o del prieto y amarillento, y me contestó que usaban ambos, pero que más se consumía allá el arroz criollo. Le interrogué, si no había sufrido alguna enfermedad anterior, contestóme que no.

Procedí a explorar los reflejos y encontré totalmente abolidos, el patelar, el rotuliano y el cremastérico, conservándose el pupilar, el olecraniano y el óculocardíaco. El mismo día hice trasladar el enfermo a una casa particular, y fué menester sacarlo en brazos para colocarlo en el auto. Ya desde el momento se establece y acentúa cada vez más, sin ceder en lo mínimo, al través de cuarenta y ocho días, un estado de inhibición permanente en todas las funciones medulares de relación, situadas por debajo del centro cilio-espinal, y que se traduce por parálisis completa, sensitiva y motora de los miembros inferiores; parálisis de la vejiga que hace indispensable el uso de la sonda para vaciarla, mañana y tarde; parálisis de los músculos del abdomen, destinados al esfuerzo de la defecación; parálisis del recto y de la S iliaca, que es preciso desocupar todos los días mecánicamente. Muy desconcertante me pareció que los esfínteres no hubiesen perdido su poder contráctil en medio a este desastre neuro-muscular. No había incontinencia rectal ni vesical; cuando se retardaba el cateterismo a la hora fijada, el enfermo orinaba por rebozamiento. No debemos sinembargo olvidar que estos músculos reciben su inervación de un plexo mixto: (el plexo sacro); su funcionalismo es a la vez que intencional y consciente, involuntario y orgánico.

Interrogando las funciones adscritas a los tres manojos nerviosos que conservan su autonomía en toda la extensión del tractus medular, encontramos que, el cerebeloso, situado superficialmente en los cordones laterales, y que parece presidir al grupo de funciones genésicas (erección, espasmos, &) y a las de acomodación y conservación del equilibrio), y el manojo simpático, llamado también de Owsjannikow, formado por una red de células policlonas, situadas a un lado y otro de la comisura posterior, y que es el núcleo de conexión y de coordinación donde se verifican los reflejos cruzados de los miembros y los demás reflejos medulares, ambos quedaron totalmente abolidos en el desempeño de sus respectivas funciones. Pero el tercer manojo, llamado piramidal directo, situado en la cara interna de las columnas anteriores, destinado a trasmitir las voliciones cerebrales para la satisfacción de aquellos actos y necesidades meramente corporales, debió quedar intacto, porque el enfermo tenía conciencia de su impulsión voluntaria, de que podía influir sobre sus esfínteres, y hacía por vencer su resistencia, pero éstos no obedecían; estaban como espasmodizados por un determinismo orgánico. Y es porque el acto muscular que opera la micción es muy complejo; en él intervienen dos géneros distintos de fibras nerviosas: unas que nacen del tercero y cuarto nervios sacros, y otras del plexo hipogástrico; la primera vía está unida al cerebro por el cordón piramidal ya mencionado, y que sube por la médula oblongata y el pedúnculo cerebral hasta la corona radiante y la corteza de los hemisferios; la otra vía la forman los nervios motores vesicales, contenidos en el plexo y que vienen de una parte muy limitada de la médula lumbar. Dispuesto así este mecanismo fisiológico, las fibras que trasmiten a la vegiga la impulsión voluntaria, es decir, las fibras motrices del esfínter, deben estar contenidas exclusivamente en el cordón cerebrosacro, sin que esto quiera decir que algunos filetes no se distribuyan por el cuerpo del órgano, como en efecto sucede; y en cuanto a las otras fibras motrices, nacidas en la médula, que llegan a la vegiga por el plexo hipogástrico y se distribuyen por los músculos expulsores de la orina, son completamente ajenas al acto voluntario. Se concibe pues perfectamente que una lesión pueda abolir la función en el centro vesicoespinal sin afectar *d'emblee*, al mismo tiempo el otro sistema motor.

En síntesis, en la inervación de la vegiga hay independencia recíproca del esfínter y de los músculos propulsores, y ello explica la doble influencia que ejerce la médula sobre la micción, y por la cual es a la vez un centro funcional y un simple agente de trasmision; así es que puede haber inercia funcional, aislada, de cada uno de los sistemas motores que entran en la inervación de la vegiga. Análogo mecanismo puede invocarse para explicar la parálisis del intestino y de los músculos que operan la exoneración, frente al espasmo del esfínter anal. Este doble trastorno se efectuó en el caso a que me vengo refiriendo. La indemnidad manifiesta del manojo trasmisor de la incitación voluntaria cerebral, se explicaría por el concurso fortuito de cierta acción exentiva, salvadora, de orden inverso a la que agrede determinadas y circunscritas regiones de la médula, en las lesiones sistematizadas.

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A todo esto hay que añadir la inhibición completa de los nervios que presiden a la todavía vaga e imprecisa función que se denomina trofoneurosis.

Derivándose de aquí un proceso agudo de atrofias y gangrenas de intensidad creciente, que se inicia por modo insólito, sin poderlo detener por ningún medio, siempre regional y tomando por punto de partida, para la atrofia, los músculos extensores y abductores de los miembros abdominales; y para las gangrenas, los sitios donde se efectúan las más ligeras presiones: región sacra (de cúbito dorsal), región de los trocánteres (de cúbito lateral), y, por último, parte interna de la estremidad inferior de los muslos, por el mero descanso momentáneo de un cóndilo sobre el otro. Y es un proceso enteramente análogo al del *Decubitus Acutus* de los antiguos autores.

La gangrena principia por la piel: ligero eritema y éxtasis vascular, luego coloración violácea en toda la zona expuesta a la presión, en cuyo centro se forman flictenas que al romperse dan salida a un líquido citrino sanguinolento; simultáneamente asfixia, circunscrita a la zona hiperemiada; pero no asfixia por isquemia, como sucede en los territorios cerebrales y pulmonares cuando se produce el foco apopléctico, por embolía; ni como la que acompaña a la gangrena simétrica de las extremidades; o la que sobreviene en los miembros, cuando no se logra restablecer la circulación colateral en la ligadura de los gruesos troncos arteriales. Aquí las arterias y arteriolas conservan íntegra su permeabilidad. Parece que se trata más bien de una astenia capilar, por parálisis de los nervios vasoconstrictores. Luego el esfacelo destruía, una por una, las distintas capas del dermis, invadía los tegidos subyacentes: tegido conjuntivo, aponeurosis, músculos, periostio, huesos, &; y era una verdadera desintegración molecular, una necrobiosis aguda que se propagaba por compenetración de los tegidos, que iban cayendo unos tras otros en putrílago, friables y disociados, como por efecto de una acción química. De tal suerte estaban muertos estos tegidos que, en las curas, que se repetían hasta dos veces por día, (pues de otro modo era insoportable la fetidez cerca del enfermo), cuando se disecaban los pingajos, para despejar el campo y facilitar la antisepcia de las cloacas subyacentes, era como si el paciente estuviese bajo el efecto de una raquianestesia o bajo el sueño clorofórmico, tan completa era la parálisis sensitiva; pero subsistía la sensibilidad consciente al calor y la tactil: el enfermo sentía el frío de los instrumentos en las curas y el calor del agua hervida con que se preparaban las soluciones antisépticas; y al pinchazo del alfiler, sentía la presión de la punta, pero sin dolor, como si fuera un cuerpo romo.

Es tan sugerente este caso, que puede ilustrar algunos puntos todavía imprecisos de fisiopatología nerviosa: como llevándonos a pensar, por ejemplo, en la existencia de otros tantos centros psicoreceptores, aun no bien estudiados, relacionados con el sensorio, y cuya autonomía queda ahora puesta de manifiesto; pues en medio al naufragio de tantas funciones, se han podido salvar éstas relativas a la sensibilidad térmica y tactil; pudiéndose colegir, desde luego, que, si quedaron indemnes, ha debido ser sin duda, porque los núcleos de origen y nervios trasmisores respectivos, quedaron situados fuera de la acción intensiva de la infección.

Lo contrario de lo que pasa ordinariamente en la siringomielia cuya lesión tiene por sitio de preferencia la región inferior de la médula cervical. Allá la sensibilidad térmica se borra progresivamente hasta no distinguir el paciente entre el frío y el calor, que quedan reemplazados por una sensación de simple contacto; y a la inversa también del caso que estudiamos, estos trastornos son particularmente frecuentes en los miembros toráxicos, en el tercio superior del tronco y en el cuello. Por lo demás, las funciones cerebrales (intelectuales y emotivas) quedaron intactas, así como las de los docee pares craneales, inclusive el neumogástrico; solo se observó un ligero grado de hipoacusia. Los actos conducentes a la producción del lenguaje: (fonacion, juego de los músculos laríngeos, y de los de la articulación, &); los que dan expresión a la fisonomía: (sinergia de los músculos faciales y oculares; los movimientos de los hombros, de los brazos, de los párpados, de rotación del cuello, contracción del músculo occipitofrontal, que, como es sabido, tienen sus centros de localización en el cerebro: (región perirolándica, circunvolución de Broca, lóbulo para-central, & &), permane.

cieron en la más completa integridad hasta unos dos o tres días antes de la muerte.

Tan circunscrito estuvo el proceso degenerativo a las regiones dorsal y lumbar, que al poner los puntos de fuego (dos veces por semana), si por acaso la punta del cauterio caía por encima de la vértebra *próminens*, sentía al punto el paciente la más viva sensación de quemadura, mientras que el resto de la columna, y por los flancos, por los lomos, por las paredes del abdomen, permanecía insensible.

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También hubo pérdida absoluta en los miembros abdominales del sentido muscular, activo y pasivo (acinecia y adiadocinecia); y pérdida del sentido articular, de las sensaciones de peso y de resistencia; hubo astereocnocia, aunque difícil de precisar en un enfermo que carecía de base de sustentación. Por el contrario, los músculos de la garganta, los del istmo de las fauces, los de la laringe y del esófago funcionaban bien.

Algunos reflejos como el bostezo, la tos y el estornudo se le hacían muy difíciles.

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Hubo taquicardia desde el primero hasta el último día (ciento veinte y hasta ciento cuarenta pulsaciones, como acontece en muchas infecciones); se lograba algunas veces reducir un tanto las palpitaciones con el estrofanto y el sulfato de esparteína. Creo que no debe atribuirse esta frecuencia del pulso a paresia del nervio frénico (nervio de Cion); más lógico nos parece pensar en una excitación o disturbio de los filetes simpáticos que recibe el corazón, o de los ganglios intracardiacos. Me lleva a suponer así la circunstancia de que, a estar el nervio vago interesado, no debía serlo única y especialmente en el ramo que le cede el espinal al nivel del ganglio plexiforme, que es de donde emerge el filete de Cion; ya que por otra parte, no se presentaron manifestaciones peculiares en todo el curso de la enfermedad, como disnea, opresión, dolor retroesternal, barra epigástrica, bola esofágica, sensación de constrición en la base del tórax (corset beribérico de Le Dantec); como también hubo indemnidad de los nervios frénicos y esplánicos; no se vieron tampoco otros síntomas reveladores del trastorno neumogástrico, como vómitos, poliuria, polaquiura, pirosis, &.

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No hubo fiebre en todo el curso de la enfermedad, tan sólo décimos de grado. No hubo congestión activa ni pasiva de las vísceras; no hubo edemas; era un caso típico de la forma seca o parapléjica; pero la gangreña era húmeda.

En su papel de filtro y como órganos eliminadores de toxinas y demás desechos orgánicos, los riñones funcionaron bien hasta el fin; y así se explica que hubiera podido durar el enfermo cuarentaiocho días. No había albúmina, siempre hubo buena cantidad de orina en la vegiga, la que se fermentaba a menudo, de modo que constantemente se practicaban lavados en dicho receptáculo, redoblando las precauciones de antisepcia al hacer el doble cateterismo diario; y a pesar de todo, siempre se tornaban amoniacales las orinas; prueba de la precaria vitalidad del reservorio.

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Estaba tan consciente el enfermo y tan creído de que podía curarse, que no quiso se llamase a ninguno de sus familiares; porque decía él, que estaban muy lejos, y quién sabe en que condiciones, para un viaje tan largo.

Sí, se le notaba cierta apatía respecto de sus necesidades corporales, hasta el punto de no reclamar nunca el alimento, y era preciso estar pendiente de hacérselo tomar; pero sí le hallaba gusto y masticaba y deglutía perfectamente. También la digestión se conservó en buen estado, y no se quejó de debilidad sino en los últimos días. La muerte debióse a hipotonia del miocardio, intoxicado.

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Cuando se le aplicaba la electricidad, (al principio débiles corrientes farádicas), decía que sentía como estremecimientos profundos en los miembros.

Estas sacudidas involuntarias con subsalto de tendones, también las sentía espontáneamente, fuera de todo estímulo externo, y este es síntoma que se observa en algunas lesiones medulares. El poder exitomotor fué disminuyendo gradualmente, apesar del aumento en la intensidad de la corriente, efecto natural de la creciente atrofia de los músculos. Esta fué acentuándose de tal modo, que en algunos puntos, en vez del relieve natural que forman las masas musculares, se veían depresiones en forma de correderas longitudinales, (región antero-externa de la pierna y del muslo).

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Seguí el tratamiento de acuerdo con las indicaciones y prescripciones que acostumbran los médicos de aquella región: tratamiento sintomático, como no podía menos de ser, no conociéndose entonces ningún suero específico, curativo, ni la vacuna preventiva. Nada dió resultado: ni los tónicos, ni los dinamósforos (extracto fluído de miurapuama (*acanthea viridis*), que tanto recomiendan los autores brasileños); ni los revulsivos, ni la electricidad, ni la estricnina, tan preconizada por los médicos regionales; ni los moderadores del corazón, ni la esparteína, calificada por Huchard, como el metrónomo del corazón; ni los eliminadores, aunque talvez a su acción se debió un tanto la prolongación de la vida del enfermo, Desde un principio pensé en el cambio de clima. que suele dar óptimos resultados; pero el estado del enfermo no se prestaba a ello. Se cambió tres veces de casa, mejorando siempre los condiciones higiénicas. El régimen dietético, que presta los mejores resultados en otras zonas, se observó aquí rigurosamente, pero sin éxito.

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Ante un caso tan extraño, caracterizado por perturbaciones fundamentales, tan marcadas y circunscritas; subitáneamente seccionado el organismo en dos porciones: la una con su funcionalismo casi normal, la otra con extinción completa de todas las funciones de relación y gran menoscabo de las de nutrición, no pude menos de evocar vivamente el recuerdo y establecer la comparación con un caso de traumatismo de la médula que tuve ocasión de observar en Coro hace ya muchos años y que se tradujo por un síndrome exactamente idéntico, con excepción del estado, de los esfínteres, que quedaron en relajación. Un proyectil de nueve milímetros se quedó encajado entre la primera y la segunda vértebra dorsal, ocasionando la sección de la médula en dicho punto. Huelga decir que el daño allá causado mecánica y brutalmente por el cuerpo extraño, lo hicieron aquí con más retardo las toxinas, los exudados y la degeneración del centro medular. El resultado ha sido el mismo: en uno y otro caso la solidaridad funcional entre el cerebro y la porción de la médula situada por debajo de la lesión, ha quedado interrumpida.

Reflexionando un poco se nos ocurre preguntar: Cómo es que se ha producido ese confinamiento del proceso morboso solo a las porciones dorsal y lumbar de la médula? La infección, como ya dijimos, se hace al través de los *vasanervorum*, debiera haber invadido pues todo el sistema nervioso, y sinembargo se ha acantonado desde un principio, sin propasarse en una línea.

Este es uno de los tantos puntos de interrogación que hay en la Medicina.

Sin duda que esto debe estar condicionado por factores ocultos, que son decisivos, y cuya esencia ignoramos hasta hoy; pero de cuya eficacia no podemos dudar. Tanto equivaldría a preguntar, (y aquí podemos elegir *ad-libitum*): ¿Porqué tiene el cálomel una acción electiva sobre el hígado? ¿Por qué se fija el curare sobre las placas terminales de los nervios motores? ¿Por qué la afinidad de la toxina diftérica por el centro velo—palatino, y la de la tetánica por los centros masticadores y la de la encefalitis epidémica por el centro de la acomodación visual, y la de la cocaína por los nervios sensitivos? ¿Por qué cuando unas toxinas producen parálisis, como la diftérica, la escarlatínica, la beribérica, &, otras producen contracturas y se localizan de preferencia en ciertos grupos musculares, como la meningocócica, la estafilococica y la que elabora el bacilus de Nicolayer? ¿Por qué las lesiones de la encefálitis epidémica se circunscriben al mesocéfalo, y unas veces es la forma letárgica y otras los síndromes mioclónicos los que prevalecen? ¿Por qué se forman anticuerpos, precipitinas, aglutininas, &, en el plasma sanguíneo, correspondiendo siempre de un modo específico, según la naturaleza del antígeno en función? ¿Por qué la excitación del seno carotídeo, (zona reflexógena), provoca bradicardia y un aumento de la tensión arterial, que puede llegar hasta producir el síncope en un momento dado?..... ...... (¿?) En el estado actual de la Ciencia, aun son muy imprecisos los límites de lo cognoscible; y hay ciertas direcciones en que tenemos por delante un campo inmenso por donde divagar largos años y andar a tientas todavía......

Ante la identidad de los trastornos, en el desconcierto patológico de estos dos casos de tan distinsa índole: el infeccioso y el traumático, que acabo de recordar, donde se vé tan manifiesta la obnubilación de los centros medulares; al recordar las lesiones centrales del beriberi, que he apuntado más atrás y que han sido verificadas al microscopio, insisto en proponer al ilustrado criterio de esa docta Corporación, la designación *polineuromielitis* para la infectotoxemia que motiva éste escrito.

J. Graterol y Morles.

P.10107
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"BERIBERI" IN CHEDUBA ISLAND, ARAKAN, BURMA.

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In the rainy season of 1929, beriberi appeared in epidemic form in Cheduba, a large island which forms a township in the Kyaukpyu district of the Arakan division of Burma.

The island, which, according to the 1921 census, had a population of 32,521, almost entirely Arakan Buddhists, lies to the south-west of Kyaukpyu Island, on the eastern boundary of the Bay of Bengal, in latitude 18°50′ N. The inhabitants are very backward; the island contains no proper roads, and internal communications are of the most primitive description, communication between the sea coast and the interior being very difficult during the rains. Apart from a few sailing boats, which carry rice to Akyab and Bassein in the open season, the only connection with the outside world is by means of a steam launch of the Arakan Flotilla Company, which calls at Cheduba village once a week, linking it with Ramree and Kyaukpyu on Kyaukpyu Island. There is no hospital, dispensary or doctor on the island, although there are several pleaders; litigation as usual having developed ahead of medicine.

The first intimation of the occurrence of the disease was received by the District Health Officer early in the month of October, and a Sub-Assistant Surgeon of the Public Health Department was despatched to Chedubá to investigate. He found on his arrival on the 12th October, that the outbreak had subsided, and, although he saw 38 cases, of which a few were not out of danger, there were no fresh cases developing, and, excepting for the deaths which had occurred, the vast majority were convalescent. He was informed that most of the cases had occurred in the months of July and August. The principal signs and symptoms he reported were loss of knee-jerks, numbness and weakness of the lower extremities, ankle drop, and œdema, principally of the lower limbs, in about 50 per cent. of cases. The only cardiac involvement he reported was " hypertrophy " in a number of cases, but later enquiries showed that palpitation was a common symptom. A noticeable feature was the strong appetite of those attacked. Most of the cases developed fairly suddenly when the men and women were out at work, and not a few were rapidly fatal. The majority of cases were among adults from 18 to 30 years old, and more men are reported to have been attacked than women.

A report by the Township Officer, Cheduba, stated that there had been 1,007 cases with 64 deaths by the end of September. Subsequent investigation has brought the total up to 1,650 cases with 188 deaths, in the period from the beginning of July up to the 5th October 1929.

The Sub-Assistant Surgeon first upon the scene visited some of the affected villages, and carried out propaganda work, with the aid of the Public Health Department's leaflet on beri-beri. He also investigated the question of diet. Rice is the staple diet, and he noted that some rice he found stored in houses was apparently mouldy, though the sample he took in a test-tube showed no sign of mould, when he examined it with a hand lens 24 hours after. Rice is stored by villagers in the "red" condition, in big bamboo baskets or bins treated externally with cow dung or internally thatched, in earthenware jars, or in wooden boxes, some of which were lined with zinc sheet, removed from the cases in which matches are packed. In the rains the rice is attacked a good deal by insects. As required for consumption the rice is hand pounded till it turns white. In addition to rice, the Sub-Assistant Surgeon found that curry was eaten, containing what he considered to be a quite inadequate supply of fish or prawns, prepared as a soup with vegetables which were deficient in quantity.

The Sub-Assistant Surgeon's conclusions were that mouldy rice was the cause of the outbreak. He formed this opinion because he considered that, if diet deficiency were the cause, the disease should not be so definitely associated with the rains. He noted that the rains had been unusually severe this season. He concluded that the people ate this mouldy rice to excess, and that the disease was due to a toxin present in the rice. He believed that towards the end of August or September, with an improvement in the weather, the rice also improved in condition; and also that the hard labour in the rice fields being over by then, the people did not eat so much of the rice, thereby reducing the amount of toxin consumed. He formed the opinion that the hand pounded rice, as used by the villagers, was not totally devoid of vitamin B.

This was the position at the end of October, and, as the outbreak had subsided and my department was fully occupied with urgent work, I postponed further enquiries till the end of the year. In November the island was visited by the Hygiene Publicity Officer, who carried out publicity work on the causes and prevention of beriberi, and in February 1930 an Epidemic Sub-Assistant Surgeon was posted to Cheduba to continue investigation, and to carry out from village to village educative work on beriberi prevention, distributing leaflets on the subject in the Burmese language among the people. In April 1930 I managed to pay a visit to the island, and to investigate conditions on the spot.

By this time a good deal of information had been collected. It had been established beyond doubt that this disease, well known to the local people under the names of *htunua*, *padarek* or *htunsketna,* is endemic in the island, and had occurred more or less severely every rainy season so long as people could remember, beginning when monsoon conditions were well established about the end of June or first week of July. It came prominently to notice in 1929 because the outbreak that year was exceptionally severe. The villages principally attacked are those along the sea coast, villages in the interior being little affected. In 1929 the outbreak began in July, became widespread in August, and subsided about the end of September. In 43 of the more heavily affected villages inspected along the north and east coasts there were 520 cases, with 101 deaths.

In 1929 the rains were unusually heavy, and the weather very rough with frequent gales and strong winds, and a good deal of flooding. Work in the fields was hard, and the people were exposed to much cold and wet.

Rice is the main crop of Cheduba. Several varieties are grown, and the island rice, particularly the variety known as *yakhine-tha-ma* which has a long slender grain, is highly esteemed and commands a high price. Much of it is exported to Akyab, Bassein and Kyaukpyu. The same kinds of rice are eaten by the people of the coastal villages as by those of the interior. The rice, being stored in village houses as red rice, is hand pounded in small quantities before use. There are no rice mills on the island and hand pounded rice is exclusively used. The villagers I have questioned do not consider that the rice became mouldy in the rains of 1929, and maintain that its taste and smell remained fresh throughout the season. The samples of hand pounded rice I saw in the houses of the people were exceptionally thoroughly decorticated for hand pounded rice. In all cases the germ was absent, and only in an occasional grain could any of the red pericarp be detected. The rice cleanings, after the rice is pounded in the wooden mortar, are given as food to cattle and hens, and the villagers have noted how well these animals thrive on them. When rice is cooked the water in which it is boiled is thrown away.

During the cold weather fresh fish is obtained in abundance, and is largely eaten by the coastal villagers; salted fish being sent inland and exchanged in great measure for vegetables and fruits with the villagers of the interior, where these are principally grown. These vegetables include several varieties of beans, peas and pulses. In the hot weather fish is still obtained in good quantity, as are also vegetables and fruits of many kinds, and groundnuts are abundant.

When the rains set in fishing stops, and the people are without fresh fish until the rains stop. At this season a few prawns are obtainable, but even salted fish is scarce and expensive. As the rainy season progresses communication with the villages of the interior becomes cut off and the supply of vegetables and fruit becomes very scarce, the people on the coast being reduced to pounded rice, a small quantity of *ngapi* (a preparation of salted fish), and a very limited supply of green vegetables, mainly in the form of the leaves of three shrubs and a few bamboo shoots. At this season the rice fields have to be ploughed and sown and the hardest outdoor work of the year takes place. The men and women, out in the fields all day, return hungry to a meal of pounded rice with a little curry stuff in the shape of a thin soup of *ngapi* with insufficient vegetables to go round. Chickens are scarce, and the villagers state that one fowl a year is about the average consumption. Eggs are also scarce, and in any case are not looked upon as a fit food for Buddhists. Milk is only used in small quantity by the well-to-do. Coconut milk becomes available in the later part of the rains.

The position as regards toddy is interesting. The local toddy is made from the *dhani* palm. It is plentiful during the cold and the hot weather, but very scarce from May to September. In June and July the supply is at its lowest, and practically ceases owing to the fact that the stem of the *dhani* blossom, from which the sap is obtained, is small and thin at this season. In the coastal villages toddy is an important article of diet. In one village I visited of 300 houses, 600 bottles of toddy a day are obtained in the autumn, and, although much is sold to other villages, the village elders informed me that all except the young children and old people drink it, and that a bottle a day is quite an usual ration at this season. The village supply of 600 bottles a day in October falls to 120 bottles by April, and dwindles to almost none by the end of May.

A consideration of all the circumstances leads me to the opinion that while mouldy rice as a possible factor cannot be entirely excluded, all the evidence points in the direction of the disease being a true beriberi due to diet deficiency. The incidence of the disease, just at the time when food is at its lowest and the diet unbalanced, and when there is strong evidence of deficiency of food-stuffs containing vitamin B; the distribution of the disease in the coastal villages, while the interior villages better supplied with vegetables, particularly of the leguminous type, escape; and the very noticeable feature of hunger unsatisfied by a carbohydrate diet, are all strongly suggestive of diet deficiency. I have previously noticed the last mentioned feature in a beriberi outbreak in 1915 in East Africa. Further, the fact that the disease clears up in the autumn when fish and vegetables again become available, though the same rice remains, supports the deficiency theory.

In the absence of doctors practising modern medicine on the island, the villagers, among whom are *Se-sayas* or practitioners of indigenous medicine based on empiricism, treated the disease by administering bull's urine, with added salt or turmeric to disguise the taste. This, as would be expected, caused purgation and diuresis, and is stated to have been of considerable benefit in the cases showing œdema. It was not so successful in the dry type. For some reason, or more probably without reason, the urine of black bulls was preferred.

Acting upon the diet deficiency hypothesis, I have arranged for extensive propaganda among the people with the object of improving their diet, particularly during the rains. All are being advised to use red rice instead of the highly pounded white rice now in use. In cases where people decline to take the red rice, they are being advised to collect the meal remaining from the hand pounding, and to consume it in the form of a porridge, or baked in cakes or biscuits. They are being advised to lay in a supply of dried peas, beans, and pulses, during the dry weather, and to keep them stored for consumption during the rains, especially in the germinated condition. They are further being advised not to throw away the water in which their rice is boiled, but to use this as a drink, or as a nucleus for their soups and curries.

In view of the apparent value of fresh toddy as a source of vitamin B, the question of the collection and storage of the excess yeast, which forms on the toddy and is at present discarded, is being examined, in the hope that it may be made use of as a protective food during the endemic season.

SUMMARY AND CONCLUSIONS.

What was at first supposed to be a new outbreak of epidemic beriberi in a remote island off the Arakan coast, has turned out to be an unusual incidence of this disease, which has long been endemic on the island.

During the rainy season of 1929 approximately 1,650 cases with 188 deaths occurred among a population of 32,500. The coastal villages suffered most, those in the interior being comparatively free.

The disease is definitely seasonal, its incidence during the rains, July and August being the months in which most cases develop.

While the occurrence of mouldy rice cannot be entirely excluded, there is very definite evidence of diet deficiency, particularly marked in the months of June, July and August. At this season white rice with a meagre and insufficient quantity of salted fish, a few green leaves and bamboo shoots, form the diet in the coastal village.

The villagers in the interior grow most of the vegetables and fruit, including beans, peas, pulses and ground-nuts, and have a sufficiency of these throughout the year.

The villagers make no use of the rice cleanings except to feed cattle and chickens. They further discard the water in which their rice is boiled.

Preventive measures to be tried include the use of red rice instead of white, the consumption by the people of rice cleanings, where rice is hand pounded, the storage of legumes in the hot weather for consumption during the months of June, July and August in the germinated form, and possibly the utilisation of toddy yeast as a food.

My thanks are due to Drs. U. Ba Shin and Kaung Mra Thoo, Sub-Assistant Surgeons of the Public Health Department, and to Dr. U. Ba Kin, Hygiene Publicity Officer, all of whose notes have been of value to me in writing this article.

With the Compliments of the
Director of Public Works [illegible]

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8

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BERI-BERI—AN INFECTED EUROPEAN CREW AT LEITH.

By Major D. G. MARSHALL, I.M.S. (Retired).

Reprinted from the Edinburgh Medical Journal. *Edinburgh and London:* Young J. Pentland, *February*, 1906.

BERI-BERI—AN INFECTED EUROPEAN CREW AT LEITH.

By Major D. G. Marshall, I.M.S. (retired), *Lecturer on Tropical Diseases in the School of Medicine of the Royal Colleges, Edinburgh.*

Recently, on the arrival of a large sailing vessel at Leith from Rangoon, it was found that of the crew, twenty-nine in number, twenty-five—namely, twenty-three Europeans and two natives—were suffering from beri-beri.

In 1901 a Commission was appointed by the Norwegian Government to inquire into the causes of the disease, and the precautions which should be taken to prevent its occurrence on board ship. The report of this Commission was translated by the Board of Trade, and submitted to a committee appointed by the Royal College of Physicians, London, for consideration and report.

The conclusion reached by this committee[1] was as follows:—"The Norwegian Report, like so many other reports on the same subject, fails to give a precise answer to the question 'What is the cause of beri-beri?' and until this question is correctly answered, such practical matters as prophylaxis and treatment must continue, as heretofore, hazy and indefinite."

To remedy this unsatisfactory state of matters, it is desirable that as much information as possible should be acquired concerning the disease. The relation of the circumstances under which this particular outbreak occurred should be of interest. The facts here recorded were ascertained from the captain of the vessel, a most intelligent and observant man, who was himself suffering from the disease on arrival at Leith, and from an examination of the ship's log.

(1) The ship was 164 days on the voyage from Rangoon to Leith, touching only at St. Helena. (2) The crew was entirely European, excepting two natives of India and one Japanese. (3) Only three Europeans and one native escaped the disease. (4) The ship left Rangoon on 16th June, and therefore during the early part of the voyage must have been exposed to the full force of the monsoon, causing the ship to be very "wet." (5) The cargo consisted of 3600 tons of rice meal.

For two years previous to leaving Rangoon for home, the ship had been carrying general cargoes in the Pacific and Indian Oceans. There had not been any marked sickness on board. After leaving Rangoon, land was not touched until, on account of the condition of the crew, the captain was obliged to put into St. Helena on 22nd September.

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[1] "Notice to Shipowners and Shipmasters," Handbill 215, Board of Trade, June 1904.

On 9th September, *e.g.* seventy-six days after leaving Rangoon, one of the crew reported sick, complaining of swelling of the legs. Two days afterwards the Japanese member of the crew was unfit for duty, with the same symptoms. He, from previous experience, was able to inform the captain that he was suffering from kakke.

On the 15th September, four other men were on the sick list; and by the time St. Helena was reached (thirteen days after the first case occurred) almost the whole of the officers and crew were suffering from the disease. The vessel remained for ten days at St. Helena. The worst cases were sent to the shore hospital for treatment; the rest kept on deck under awnings.

On 1st October, the sick men having been sent back from hospital, the voyage was resumed, all the crew except two being (according to the log) fit for duty. During the two months' voyage to Leith there were several severe relapses, the first mate in particular being most seriously ill with cardiac symptoms. But eventually the ship was docked at Leith on 30th November, with the crew complete, none of the cases having ended fatally, but all the officers and most of the men still showed marked signs of the disease.

In contrast to this, the captain informed us that while they were lying at St. Helena, two other sailing vessels called there with beri-beri among the crew; in the one case, two men and the first mate, and in the other, eight of the crew, had died of the disease.

EXAMINATION OF OFFICERS AND CREW.—The crew were paid off directly the ship arrived, and there was little opportunity for examining them. It was noted, however, that a large proportion still showed signs of œdema.

The captain and first and third mates remained on board, and were carefully examined. The first named was found to be suffering from dilated heart; he walked with a hobbling gait, and exhibited all the usual signs of peripheral neuritis associated with beri-beri, especially in the left leg. There was marked anæsthesia and analgesia over most of the limb, but especially on the inner side of the foot and leg. About 3 in. above the ankle, completely surrounding the limb, was an area about an inch wide over which the most exquisite hyperæsthesia existed. The knee jerk on the left side was very much impaired.

The first mate still presented signs of œdema of the face, but was practically well. The third mate, one of the cases removed to hospital at St. Helena, still suffered from cardiac affection. There was epigastric pulsation, marked increase of dulness to the right, and, on auscultation, a peculiar irregular action, with systolic bruits and reduplication of the second sound at the base.

The crew appear to have chiefly suffered from œdema of the lower extremities, extending upward to the chest; none of them had œdema of the face. A large proportion suffered from cardiac symptoms, and were rendered unfit for duty, not from symptoms of paresis, but from being, as expressed in the log, "short winded."

In view of Hamilton Wright's theory that the primary lesion is in the stomach and duodenum, careful inquiries were made to ascertain if the onset of the œdema had been preceded by gastric symptoms. This was found to be the case, the men attributing their dyspeptic symptoms to the water, which, though perfectly clear when put on board at Rangoon, very soon turned a "dirty yellow colour."

It may be well to state very briefly the various theories which have been advanced regarding the cause of beri-beri, and to consider if any of them would assist in determining the cause of this particular outbreak. The causes assigned may be divided into predisposing and exciting.

PREDISPOSING.—*Heat, moisture, and overcrowding.*—It is generally admitted that these factors influence the onset and spread of the disease. It is more prevalent in tropical and sub-tropical regions during hot moist weather, and often breaks out in the forecastles of ships coming from hot climates through overheating on reaching colder climates.

The temperature on board this ship during the monsoon was doubtless high, and, owing to the rough weather experienced, it was also damp, but there was no overcrowding in the forecastle, which was particularly airy and dry, and the quarters occupied by the officers were very dry and spacious.

A place disease.—This may be set aside in this case. The ship had been in the tropics for two years without any cases of beri-beri. It is interesting, however, to note that previously two other captains of the vessel had suffered from beri-beri while on board.

Want of nitrogenous matter and fat in the food.—The dietary was ample, and in excess of the Board of Trade requirements.

Want of fresh vegetables.—This is a cause often overlooked. A sailing ship cannot carry a supply of fresh vegetables sufficient for a voyage of three or four months, and lime juice and preserved vegetables are indifferent substitutes. There was marked improvement in all the cases when St. Helena was reached and a plentiful supply of vegetables obtained.

The Norwegian report quotes cases of the occurrence of beri-beri on board ships which had not been in the "endemic" area, or had any connection with infected parts. The London Commission was apparently sceptical on this point, but it is well known that cases of beri-beri are not infrequent on whalers when calling at St. Helena on their return from the south.

The influence of race.—As a rule, Europeans are less liable to attack than natives, but this case shows that, given the necessary conditions, they may suffer equally with natives.

EXCITING CAUSES.—There are many theories regarding the cause of the disease. Some, as those which ascribe it to the consumption of stale or infected fish, or class it as a form of arsenical poisoning, need not be considered. Those worthy of consideration are—(1) The germ theory; (2) the toxin theory; (3) the rice theory; (4) the part played by insects.

Germs.—Several have been described as the active agent. Pekelharing and Winkler described a bacillus which they credited with a curious attribute, *e.g.*, that repeated infection by the bacillus was necessary to maintain the disease; they are said to have reproduced the disease by infection of lower animals with the bacillus. This view is not generally accepted. The Board of Trade advise restrictions in the use of tinned food, "70 to 80 per cent. of various kinds having been found to contain ~~visible~~ viable microbes."

Toxins.—Hamilton Wright, who has spent several years investigating the disease in the Malay Peninsula,[1] considers that the disease is due to a micro-organism which affects the stomach and duodenum, and, forming a primary lesion there, elaborates toxins which by dissemination throughout the body subsequently produce the nerve symptoms. In this respect he draws an analogy between this disease and diphtheria. He further states that the bacillus leaving the body in the fæces is re-introduced, not by any particular kind of food, but by food contaminated by contact with fæcally polluted fingers or clothing. Unfortunately the bacillus is still a hypothetical one, as Wright has not been able to demonstrate its presence. Everything points to the disease being due to toxic matter of some kind, but whether it is elaborated by a micro-organism or not is at present pure conjecture.

Regarding the outbreak at present under consideration, whether the bacillus was present or not, fæcal contamination of the food may, owing to the perfect sanitary arrangements on board, be set aside.

The rice theory.—The disease is specially prevalent in countries where rice forms a staple article of diet, and the possible connection between the consumption of mouldy or otherwise impure rice and the incidence of the disease has long been recognised. Lately, Travers, Wright, and others have endeavoured to prove, by extensive experiments on the feeding of prisoners, that this connection does not exist. On the other hand, other observers have brought forward instances to show that the disease may be due to the presence of either fungi or organisms in the rice, with the formation of ptomaines or toxins. This is recognised in ergotism and pellagra.

Clarke,[2] in the discussion on beri-beri at the last meeting of the British Medical Association, showed that Tamils do not suffer from beri-beri even when living in a country where this disease causes one-third of the total deaths. He ascribes this to the fact that they boil their rice before husking it, while the Chinese use rice which has been husked raw, and may be "contaminated by a poison which lies in the husk."

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[1] *Journ. Hyg.*, 1905, April; *Journ. Trop. Med.*, 1905, June 1; *Brit. Med. Journ.*, London, 1905, October 25.

[2] *Brit. Med. Journ.*, London, 1905, November 11.

The part played by insects.—It has been suggested that the virus of beri-beri may, as in yellow fever and other diseases, require an intermediate host for its proper development. Little work has been done in this direction, excepting a few inconclusive experiments with the ordinary bed bug, but it is quite possible that weevils (calandra-olyzar), beetles, cockroaches, and other insects may play a part either in the development of the active agent, or by acting as mechanical carriers of the infection.

"Rice meal," with which this vessel was loaded, is not, as the name would imply, a meal prepared by grinding rice, but is simply the husks and residue left in the process of husking; it is imported into this country to be used in the manufacture of feeding cake or cattle. When the hatches were opened, a most sickly, disagreeable odour was very apparent. The outer surface of the bags in which the meal was contained was covered with countless crawling insects, and a sample of meal taken at random showed them in large numbers. They were to be seen in all parts of the ship. Even in the officers' cabin they could be swept from the oor in handfuls. On examination, they were found to be small beetles about a quarter of an inch long. A thorough search of the ship for other insects was made by Mr. Evans, of the Natural History Department of the University, who has kindly furnished me with the subjoined list. It would be interesting to know if the presence of any of these insects has before been noted in connection with outbreaks of beri-beri.

1. Beetles.—*Tribolium ferrugineum F.*, in enormous numbers, on ıgs, and all over ship. *Alphitobius piceus OL.*, plentiful. *Lathelicus ryzæ Wat.*, in small numbers.
2. Cockroach.—*Periplaneta Americana*, in large numbers.
3. Moth.—*Tineid*, species not determined; numerous.
4. Spider.—Not yet identified, common in dark corners about roof the hold.

Conclusions.—The ship apparently became infected at Ran-oon, but whether by an ambulatory case, or infected food, or ırgo shipped at that port, is an open question.

The fact that both officers and men were affected points to ome conditions on board common to all. These were—(1) Water ıpply, (2) weather conditions, (3) nature of cargo, (4) food ıpply.

(1) and (2) may be set aside—it is generally admitted that the sease is not carried by water; and the weather conditions, while ıey might tend to the spread of the disease, could not originate it.

(3) and (4). In an endeavour to account for this outbreak, which, owing to the number of Europeans affected, is somewhat unique, it is impossible to overlook the probability of its being due to the nature of the cargo and the presence of such enormous numbers of insects.

The food may have been infected when taken on board, and later it was probably infected by the insects, as, owing to their invasion of all parts of the ship, it was impossible to keep the food free from them.

I am indebted to Dr. Robertson, Medical Officer of Health at Leith, for affording me every opportunity of investigating the outbreak.

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9

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September 24th, 1898.

ON BERI-BERI OCCURRING IN TEMPERATE CLIMATES.

Being a Paper read in the Section of Tropical Diseases at the Annual Meeting of the British Medical Association held in Edinburgh, July, 1898.

By CONOLLY NORMAN, F.R.C.P.I.,
Medical Superintendent, Richmond Asylum, Dublin.

Distribution of Beri-beri in the Tropics.—Of the many puzzling questions connected with the disease now commonly known as beri-beri, not the least difficult is the question of its distribution. This difficulty is not confined to countries where it is new.

Ceylon.—There seems to be no doubt that it was formerly one of the most prevalent and destructive diseases in Ceylon. It is now—though not unknown—comparatively rare in that country.

China.—In China, where in early times it was one of the most frequent diseases, it has in recent years declined to such a degree that Scheube was able to affirm that it appears now to have almost died out. That such is not the case we know through the labours of Manson; but, still, there has evidently been a remarkable ebb in the disease in that country.

Japan.—On the other hand, it would appear to be increasing in Japan. According to Japanese writers it was almost confined to the chief towns Tokio and Kioto at the beginning of the current century. Since then it has spread not only to the other great towns and seaports, but to the interior of the country, and to comparatively high levels. According to Grimm beri-beri has made remarkable strides since 1880 in the northernmost island of the group, Yezo. On the other hand, the southernmost island, Kiushiu, now presents the fewest cases and of the most favourable type.

Brazil.—The history of Brazil with regard to beri-beri is most remarkable. Almost simultaneously with the Batavian observer, Bontius, who, writing in 1642, was the first European to describe beri-beri, Piso in 1648 described an evidently identical affection as among the common chronic diseases of that country. Though attention was drawn early in the present century to the fact that a disease locally known as "airs" was probably beri-beri, the physicians of Brazil seem to have given little thought to the matter until Da Silva Lima recognised beri-beri in the epidemic of 1863. If the disease existed in the interval between Piso and Da Silva Lima in anything resembling the type which prevailed between 1863 and 1866, when the mortality among those attacked was 74.5 per cent., it is impossible to think that the affection can have been overlooked. So that we are led to believe that, if it did not wholly die out, it only existed in a mild form and to no great numerical extent.

No plausible explanation of this ebb and flow in the prevalence of this disease has ever been offered as far as I am aware.

New Epidemics.—Within recent years beri-beri is supposed to have appeared for the first time in Manila (in 1882), in Penang, in New Caledonia, and in the Fiji Islands. Besides spontaneous outbreaks, Fiji is liable to the importation of beri-beri through Hindu and Japanese coolies. Beri-beri has been frequently observed of late years in Australia (New South Wales), but I understand chiefly, if not altogether, among sailors and Chinese labourers. Under similar conditions it is reported from New Zealand. It has occurred of recent years in Natal. My friend, Dr. Hyslop, of the Pietermaritzburg Asylum, informs me that it is not infrequent in that town, and prevails not only among coolie labourers, but also among European settlers. It has been generally observed to occur chiefly on the coast in various countries or along the course of great rivers. On the other hand it has prevailed in Central India, in Assam, in Paraguay, and in the great central province of Brazil known as Matto Grosso. Some allowance must also be made for the fact that in many parts of the East only the coasts are known to European observers.

On the whole, though Japan and the Malayan Archipelago may be described as the headquarters of the disease, it is nevertheless found in very many tropical and subtropical countries, and in several of these it seems to be now spreading.

Beri-beri in Cold and Temperate Climates.—In temperate climates European and American observers have until 1894 chiefly observed beri-beri in Lascar sailors, or in Europeans who have just returned from some tropical station where it prevails. Manson has recorded cases which appeared for the first time in the Port of London, developing among Asiatic crews of vessels that had been lying up there for several months; and a very interesting account has been given by Dr. J. S. Jameson of an outbreak of beri-beri among the Lascar crew of an outward bound vessel running from Liverpool to Rangoon. The disease appeared a day or two after leaving port.

It may be held that small isolated epidemics of this kind are not inconsistent with the generally received idea of beri-beri as a tropical disease. But there are reasons for thinking that the limitation implied in the term "tropical disease" is not properly applicable to beri-beri. In the East, according to Manson, beri-beri has been observed as far north as Saghalien. That island lies between degrees 46 N. and 54 N., ranging roughly parallel with England as far north as Leeds, and France as far south as Lyons, but its winter temperature is arctic, and its mean annual temperature is about that of the northern extremity of the Scandinavian peninsula. Grimm, in his *Clinical Observations on Beri-Beri* (Berlin, 1897) combats the idea that this disease is a tropical one. His statements are very direct. He says, "We have repeatedly opposed the notion of the geographical limitations of beri-beri, and we are not now prepared to recede from our opinion—namely, that it is as little a tropical disease as leprosy. Our own observations, and those of others, have established that it appears in many thousands of cases in Yezo, the most northern of the great islands of Japan, with a thoroughly temperate climate, and a cold winter lasting for six or seven months." He speaks also of the outbreak of the epidemics which he has there observed in severe winters, when there was deep snow and a temperature as low as 15° below zero (Centigrade). Again, in the west, an affection apparently identical with beri-beri, has been observed in an epidemic form among the New England fishermen off the Newfoundland coast, as Putnam has recorded.

An epidemic of scorbutus has been described, which occurred among the French troops round Paris during the siege, and which in some cases was accompanied by symptoms resembling beri-beri. The consensus of French opinion, however, appears to have been that these cases were not true beri-beri. I may venture to say that from the descriptions given I am inclined to adopt this view.

Epidemics identified as beri-beri occurred at the Richmond Asylum, Dublin, in the summer of the year 1894, and again in 1896, and again in 1897; at the Suffolk County Asylum, Melton, Suffolk, in the winter of 1894-5, and in 1896-7; at the Alabama State Asylum, Tuscaloosa, Alabama, U.S.A., in 1895, and in 1896; and at the Arkansas State Asylum, Little Rock, Arkansas, U.S.A., in 1895. The association of these epidemics in time and by the nature of the institutions in which they broke out, is very singular. The earliest and the most serious was that occurring in Dublin in 1894.

Besides these, two cases of a form of peripheral neuritis, strongly resembling beri-beri (though not so called) have been reported by Orthmann as having occurred among nurses in the Grafenburg Asylum in North Germany in 1897,[1] and Tippel mentions similar cases from the well-known asylum at Alt Scherbitz, near Leipzig. These cases were all suspected to be due to malaria, and those occurring at Alt Scherbitz were associated with disturbance of the soil for the purpose of laying foundations for new buildings.

General Description of the Epidemics which occurred at the Richmond Asylum, Dublin.—In order to enable my hearers to discuss the nature of the disease which appeared among my patients in Dublin, I shall briefly describe its phenomena. The first condition observed was usually œdema occurring over the front of the tibia. The insane do not complain as other men do, but tenderness on deep pressure was generally early noticeable. A certain amount of superficial anæsthesia could be usually made out. Those who could and did explain their feelings generally at this stage complained of cramps in the calf muscles, and also of a greater or less degree of painful formication or a distressing sense of numbness. Always in some stage of the ailment, and usually, from the very first, cardiac disturbance made itself evident. Dealing, as often happened, with large numbers of occurring cases, we based our diagnosis roughly on this combination: (1) Œdema of the shins, without albuminuria; (2) tachycardia and cardiac irregularity; (3) pains in the legs; (4) anæsthesia of the integuments of the legs. Of these it was somewhat difficult, owing to the mental condition of our people, to estimate the degree of pain, etc., and often impossible to be sure of the existence of anæsthesia.

The cardiac conditions were somewhat variable. The most constant was extraordinary irritability, very slight exertion causing an alarming acceleration of pace; tachycardia, irrespective of exertion, was general; there was frequently a singular condition which I call unconformability of heart and pulse; thus the heart was bounding with a seemingly strong impulse and the pulse extremely feeble; spontaneous variations in the rhythm of the heart sounds occurred; bounding action with visible heaving of the chest was not uncommon; the area of cardiac dulness was commonly increased, especially to the right; this increase often appeared with extreme suddenness; in some cases tic-tac sounds replaced the normal order, particularly when the heart was accelerated after slight exertion; the second pulmonary sound was usually accentuated at the apex; reduplications were frequent, generally of the second sound at apex producing a sort of triple sound, occasionally also of the first; occasionally *bruits* were audible of a variable and inconstant character, the most common a soft blowing murmur over pulmonary area, less frequently a *bruit* with first sound at apex sometimes only appearing after exertion. Præcordial weight and anxiety were not rare even in mild cases. Similarly, breathing was usually quickened with oppression. Sense of weight in the stomach region was often complained of. Vomiting occurred in about 5 per cent. of all cases. In the first epidemic it generally ushered in a fatal termination; in the later it did not seem to have this significance. A few cases were preceded by vomiting and sometimes diarrhœa, but this concurrence was rare. Loss or impairment of voice occasionally occurred. Sometimes even in favourable cases there was an inability to cough deeply or to sneeze. The respiration was often thoracic, apparently from feeble action of the diaphragm.

Motor Symptoms.—The first and most remarkable was loss of power in the peroneal muscles and the flexors of the foot; as a result there was almost invariably a tendency to drop and invert the foot. In advancing cases all the leg muscles became affected. The engagement of the gait was very various; most patients walked slowly and swayingly, some attributing this condition, perhaps correctly, to mere pain, others complaining of "weakness in the legs," which rendered them unable to use them freely. Occasionally the patient's gait was to all appearance perfectly normal.

A very common condition which seemed to give the most characteristic gait was a tendency to raise the feet very high in order to enable the dropped and powerless toes to clear the ground; the foot was then flopped heavily on to the ground, something after the manner of a tabetic patient, and as the patient leaned upon the foot he swayed backwards and forwards unsteadily. This condition, which was very well marked in a number of patients, is, I think, identical with that which occurs in the very common condition of pressure interference with the sciatic, which we know as the leg "going to sleep." It was occasionally mixed with and obscured by other symptoms. Thus, one patient, whose photograph is submitted, lifted and planted one foot just in the way described, while he added on the other side a slight tendency to drag the foot laterally like a hemiplegic.

In a small number of cases the muscles of the forearm and arm were tender and the power of extension was impaired; the grasp was often feeble (dynamometer). Actual drop-wrist occurred in less than 1 per cent. of all our cases, and was only extreme in one case.

The extensors of the thigh were often paralysed. Many patients when sitting on the floor could not get up without help. One or two who were restless used to progress along the floor by sitting on the buttocks and helping themselves along by the hands. Several used to help themselves into bed in this way, and when they had got their hips on the bed used to swing themselves round so as to get their lower extremities into bed without any movement of the muscles of the thigh. Patients who were getting ill of this condition, or who were convalescing again, were often noticed to be unable to stoop without collapsing. They could stand quite straight, but as soon as the knee was bent they sank down through impairment of the quadriceps. A general muscular feebleness with unwillingness for exertion of any kind was common. The calf, and occasionally other muscles, often presented in the earlier stages a hard feeling. This was sometimes limited to peculiar longitudinal masses, especially on the outer head of the gastrocnemius. Later on in atrophic cases the muscles became of course not only small, but soft.

In one case unilateral paralysis of the third nerve occurred, ptosis, dilatation of the pupil, and external strabismus.

Tendency to contractures in the paralysed lower extremities appeared in about half a dozen cases, and was sometimes difficult to deal with owing to the patient's mental state. However, only two patients have remained crippled from this condition. A very interesting, constant, and well-marked condition was extreme relaxation of the joints, especially knee and ankle, due no doubt in part to muscular wasting, but also apparently to a relaxed condition of the ligaments.

Sensibility.—In the sane the first symptom of the disease was often a sense of weariness in the calf muscles; patients complained of weakness and heaviness of the feet; cramps were frequent, and numbness. My head nurse found that she could not feel her soles on her bicycle pedals, nor distinctly her pen in her hand; stinging, burning, boring pains were present most commonly in the skin of the legs. A very frequent complaint was a sensation like the stinging of nettles. Some patients complained of pains in the soles of their feet; one said he felt as if his feet were plunged in hot lime.

Aching in the muscles was complained of in some cases, and sometimes was very severe. Occasionally there were pains shooting down the limbs. But the most frequent spontaneous complaint was of pain as if insects were creeping over a sore surface (painful formication, the *pirri-pirri* of the Japanese). A nurse suffered agonies from this condition.

Cutaneous anæsthesia was mixed up with various paræsthesiæ. A very common condition was the existence of insensibility to a very gentle touch (the drawing of a pencil lightly over the skin), while firmer pressure on the same area caused pain of a formicating character. We often noticed a phenomenon—as far as I am aware not before described, namely, the existence around each zone of hypoæsthesia (as Scheube calls it) of a zone of very distinct hyperæsthesia. In some cases, sensations of numbness, impaired recognition of objects, distances, etc., were accompanied by pain.

Anæsthetic or hyperæsthetic patches and tracts were found in various cases in many parts of the body, though they were most frequent on the legs, where also they mostly first appeared, but they were found on the thighs, on the trunk, on the upper extremities, on the nucha, and on the face. In two cases isolated patches of anæsthesia were found on the lips. They sometimes lasted for a considerable period, seemed to spread gradually, and to decrease gradually. More frequently they varied a little daily, and often disappeared with curious rapidity. In some cases the painful formication, often associated with anæsthesia, was worst at night. The fugacious and variable nature of the anæsthesia in some cases was often noted, and more than once we have confirmed the curious observation of Scheube that it is sometimes to be found only in the morning, disappearing again in the evening.

The calf muscles were always found tender on deep pressure, save in those whose mental condition precluded the possibility of testing. The superficial nerves were tender, sometimes exceedingly so. This condition was specially observable on the peroneal nerve, pressure on which almost always caused wincing.

At the suggestion of my Dutch friends, Drs. Verschuur and Eysellsteyn, we tested a few cases for anæsthesia of the pharynx, and found it always present. The reflexes, both superficial and deep, were generally exaggerated in any cases which came under observation early. As the case progressed, the knee-jerks usually became diminished, not always equally on both sides, and when there was marked loss of power they were always abolished.

Muscular Atrophy.—In a few cases atrophy appeared when there had been no œdema observed, but generally it was noticed when œdema passed off. In some cases, again, there was slight and fugacious œdema, and some little time later atrophy was observable. I suspect in no case was œdema absent, but in slight cases it did not attract attention, and the earliest condition noticed was loss of power with wasting. However beginning, the atrophy was often very marked, the wasted muscles being soft and flabby. Some of the photographs shown exhibit conditions of very marked wasting in cases also photographed in the dropsical state.

Œdema.—Œdema was, I believe, a constant condition, though in a few cases it was very slight at first or even escaped attention, and the patient appeared to pass directly into the "dry" or atrophic state. In slight cases and in early cases it was most marked along the inner side of the tibia, forming the pear-shaped swelling of Pekelharing. Less constantly the feet and legs generally were swollen. Œdema could usually be detected also over the sacrum, often over the sternum or ribs, over the ulnar border of the forearm, and not infrequently, even in slight cases, the face was puffy. Some cases presented general anasarca, often extreme. Œdema of the lungs was common, and hydropericardium and hydropleura also occurred. The superficial œdema was curiously variable: in some cases pitting was readily produced, in others there was doughy, myxœdematoid condition with much swelling and little pitting. In marked cases the œdema was sometimes noted to shift with posture more readily than is common in other forms of anasarca. It also disappeared in some cases with singular rapidity. Œdema of the fundus oculi was found in some cases by my friend, Dr. Swanzy, who was so good as to examine some of my patients. There was occasionally slight effusion into the joints, particularly the knee.

Course of the Cases.—Usually the cases began insidiously. In the sane a feeling a weariness in the legs, with occasional cramps, often preceded more definite symptoms for a considerable time. It was generally difficult to obtain evidence of prodromal symptoms among the insane. Sometimes the earlier symptoms were accompanied by a smart rise of temperature, but this soon subsided. Two cases began during convalescence from typhoid, and several patients were attacked after recovery from dysentery. The course of the affection was extremely variable in different cases. Sometimes it was steady, much more often jerky. Quite characteristic were the features observed in other epidemics of beri-beri: sudden changes for the worse in cases which were apparently doing well; extreme frequency of relapse; occasional quite sudden deaths, not infrequently occurring when convalescence had been apparently progressing favourably. The length of an attack was perfectly uncertain: on the whole the severer cases of the first epidemic tended to terminate, either favourably or the reverse, more quickly than the milder cases of the later epidemics. Speaking generally, the cases tended in the early stage to increasing dropsy and increasing loss of power, then the dropsy passed off and marked muscular wasting was apparent, which again gradually became rectified, paralysis and anæsthesia passing off at the same time. Death occurred in a variety of ways. That terrible condition, so often described in connection with beri-beri, known to the Japanese as "shiyo-shin," and apparently dependent upon failure of an overworked and weakened heart, carried off several patients, after longer or shorter periods, often coming on with fulminating rapidity, of extreme suffering (restlessness, vomiting, violent pulsation of heart, dyspnœa, cyanosis, orthopnœa, etc.). Death was often due apparently chiefly to œdema of the lungs. Syncope, apparently due to degeneration of heart muscle (found after death) was not a rare cause of death. Sometimes, as mentioned, this mode of death occurred in a case which had been apparently convalescing. Hydropericardium and hydropleura probably contributed to an unfavourable termination in several cases. In some cases mere general exhaustion seemed to be the immediate cause of death. This occurred particularly among the old and debilitated. Sufferers from beri-beri readily succumbed to other diseases. Paralysis of the respiratory muscles, particularly the diaphragm, alone or in combination with heart failure, sometimes caused death.

Electrical Reactions.—With regard to electrical reactions we are not in a position to add any evidence to the statement of Pekelharing and Winckler that it is possible to make the diagnosis of beri-beri before the advent of œdema by means of electricity, because almost every case which has occurred in the Richmond Asylum has been first brought under our notice by the observation of œdema. In some cases we could not detect any electrical change.

There were many cases where the electrical changes were very small, and in many the electrical changes disappear early in recovery. The heart symptoms may still persist when the electrical changes are no longer to be observed. In this our observations confirm what has been observed by Zwardemaaker and Krafft, that the electrical changes often disappear long before the heart trouble.

There were many cases in which no abnormality was to be observed, but that to galvanic stimulation the contractions were slow and the latent period long, the changes being only of a quantitative nature. For instance, KOC could not be obtained without giving more pain than could be borne.

The cases in which there was marked atrophy of the muscles showed reaction of degeneration. Thus the reaction of nerve to faradism was completely lost, and the reaction of nerve to galvanism was completely lost, while the reaction of muscle to faradism was lost, and the reaction of muscle to galvanism showed polar changes.

No electrical changes were observed in muscle or nerve of the upper extremities. The trapezius was not examined.

Post-mortem Appearances.—It is unnecessary to mention the less essential changes, or those common to many dropsical affections. Nothing distinctive was found in the brain or cord. The peripheral nerves (branches of vagus, phrenic, peronei, etc.) showed parenchymatous degeneration, with, in some cases, a slight degree of interstitial inflammatory change. The heart muscle almost invariably showed fatty changes, sometimes extremely well marked. The muscles of the extremities which had been involved showed granular degeneration.

With regard to the bacteriology of the disease, I am sorry to say our results were on the whole negative. We believed at first that we had succeeded in isolating a coccus resembling that described by Pekelharing; but there are reasons to believe that we were mistaken in this particular, and our results were certainly not constant.

History of the Several Epidemics.—The first epidemic occurred in 1894. The precise period of its outbreak is doubtful. I am sure that at first many mild cases were overlooked and many cases were misunderstood. I may perhaps be pardoned for pointing out that similar mistakes occur among those who first see beri-beri even in its recognised habitats and in a sane population. In the year 1894, the average daily number of patients resident in the asylum was 1,503. During the year 174 cases of beri-beri were registered; of these, 127 were male and 47 female patients. No members of the staff (sane persons) were attacked in 1894. The monthly distribution of the occurring cases showed that they increased, gradually at first and then more rapidly, from June to September, and then decreased rapidly in October, after which month no fresh cases occurred. Eighteen male and seven female patients were registered as dying from this cause. I believe that, for a reason suggested above, all these figures represent a considerable underestimate. Taking the figures as they stand, however, they show that 14.3 per cent. of those attacked died. No fresh cases occurred during the year 1895.

In the year 1896 the daily average number of patients residents was 1,686. Beri-beri reappeared in July, and increased till September. Cases continued to occur until the end of the year. The total number attacked was 114, being 31 male and 76 female patients, with 7 (sane) nurses. Two male and 6 female patients (about 7 per cent. of those attacked) died. None of the nurses died.

In 1897, with an average insane population of 1,800, there occurred 246 cases, 47 male and 199 female. Among these were 2 male attendants and 6 nurses (8 of the sane staff). None of the staff died. The deaths numbered 11, 3 males and 8 females (4.4 per cent. of those attacked). Four cases, which ought properly to be reckoned in the previous epidemic, occurred in January; then none occurred till June, 134 occurred in July, 50 in August, 7 in September, 3 in October, 37 in November, and 6 in December. The three epidemics show a total of 534 recorded cases, with 44 deaths (equal to 8.23 per cent.).

The following remarks must be made: (1) It must not be forgotten that the record for 1894 is an underestimate. (2)

The epidemic of 1896 extended into the following year, and would perhaps better be described as beginning in the July of 1896, and ending in the February of 1897. (3) The epidemic of 1894 attacked more males than females, as is usual with beri-beri. This proportion was reversed in the following epidemics.

There were remarkable differences between the three epidemics. In the first there was high mortality, *shiyo-shin* was common, there were a large number of cases of general, well-marked œdema, and motor paralysis was pronounced. In the second mortality was lower, *shiyo-shin* rare, general anasarca, though it occurred, was infrequent, and motor troubles were less marked. In the third the great majority of the cases were of that mild type which Scheube calls rudimentary; general anasarca scarcely occurred; loss of power of walking was very rare; but there was a quite special tendency to the occurrence of painful formication (*pirri-pirri*); yet in each of the later epidemics there were cases—often cases of relapse—which recalled the conditions prevalent in the first. It has often been observed how much various epidemics of beri-beri differ from each other. Mortality appears to range from 2.5 per cent. (Bälz) to 74.5 per cent. (Da Silva Lima). It has often been noted that the first epidemic at any given place is the worst, and that as the disease tends to become endemic it grows milder. Notably this has been observed in the Straits Settlements.

Local Causes.—The etiology of these epidemics remains obscure. There is no reason to believe that the disease was personally imported. It does not appear to have broken out elsewhere in Dublin either before or during its prevalence in the asylum. The Richmond Asylum is the asylum for the insane poor of the city of Dublin and the counties of Wicklow and Louth, and the patients from the city form about three-fifths of the whole. The older part of the buildings, now reserved for women, dates mostly from 1814; the newer part (male asylum) is about forty-five years old. The institution stands on about fifty-nine acres of ground. It is entirely within the city boundary. Portions are closely surrounded by the dense habitations of the poor, and in immediate contiguity with the older part stand a large public hospital, a great work-house, and a prison. The buildings stand relatively high, at levels varying from 90 to 120 feet above the mean level of the estuary of the river Liffey, on which the city is built. The surface soil is shallow, and consists largely of "made earth." The subsoil is the prevailing boulder clay of the neighbourhood, a clay formed chiefly by trituration of the middle limestone, containing many beautiful specimens of ice-worn boulders, but in the mass tough and impervious.

The hygienic condition of the asylum had been in some respects bad. Consumption was very unduly prevalent. Other zymotic diseases of various forms were rarely absent altogether. Dysentery, once a very prevalent disease in Ireland, little known there for the last forty years, a scourge in the old asylums everywhere, happily rare in modern asylums, seems to have always remained prevalent in the Richmond Asylum. This I attributed to the condition of the sewerage of the buildings, which was in the worst state imaginable, and in consequence of the representations which I made on my appointment as medical superintendent of the institution in the year 1886, an entirely new system of drainage was adopted on good modern principles. Nevertheless, some more or less permanent injury appeared to have been done through saturation of the soil under and round the buildings with sewage, because although the death-rate declined for a time and dysentery became less frequent, the improvements in either respect did not continue.

The institution had been overcrowded since at least 1886. It is difficult to set forth in precise figures the extent of overcrowding which existed, as all kinds of makeshifts were adopted to increase accommodation, but it may be briefly said that the officially-recognised accommodation of the asylum in the beginning of 1894 was 1,100, and this was admittedly an overestimate, the full population for the space contained in the buildings being about 1,000. At the same date the actual population was 1,498. Roughly speaking, the population exceeded the due accommodation in the ratio of 3 to 2. As the insane probably require more room than any other folk, this represents a very deplorable state of things. It may be briefly said that the staff were nearly as much crowded as the patients, and that all the offices (stores, kitchen, laundry, and the like) were faulty in construction and quite insufficient in size, so that workers there were crowded and huddled together in a very insanitary way.

Through large portions of the institution the arrangements for ventilation were very imperfect, the window frames being made of iron and only opening a very little way.

The floors were largely so defective that it was impossible to wax and polish them as is usual in most asylums nowadays, and they were consequently often damp from constant washing in our humid climate.

Administrative reasons necessitating the treatment of certain classes—the sick and the epileptic for example—in separate wards, these wards, originally badly enough constructed, became overcrowded to a degree disproportionate to the rest of the buildings.

The water supply is the common supply of Dublin city, and is good and abundant. It is not spoiled by being stored in tanks, and it has often been tested as drawn from the taps, and has been found to be of the best quality.

With reference to diet, there is nothing to suggest a dietetic cause. In the first place, the inmates of the asylum get no food which is not in common use in the city of Dublin generally. Again, the dietary which was always a little ahead of that given in many Irish asylums and had been improved of late years, was in 1894 good and sufficient. Each patient received as ordinary diet ½lb. bread and 1 pint of tea for breakfast and the same amount of bread with cocoa for supper. Dinner consisted of 8 oz. for men and 7 oz. for women of cooked fresh beef five days in the week, the same amount of bacon on one day in the week. The supply of vegetables was abundant, being computed at 1lb. of potatoes daily and 1lb. of other vegetables, cabbage, etc. Rice was little used, practically only as a medical extra. The decorticated variety which is that commonly sold in the city of Dublin was the kind in use. One change had occurred in the beginning of the year 1894. Half a pound of dried ling for each patient had been added to the dinner for Friday (heretofore merely bread and coffee). Dried ling, probably coming from Newfoundland, where beriberi is perhaps endemic, might be suspected, but the bulk of the working people in Dublin use just the same fish for their Friday dinner. Besides, by an odd chance it happened that for certain administrative reasons it was impossible to give a fish dinner at that time in the epileptic wards and proportionately more cases occurred in the 1894 epidemic in the epileptic wards than anywhere else.[2] Finally, towards the close of 1894, fresh native fish was substituted for imported ling, and this fresh fish has been continued since; nevertheless beri-beri after being absent for a year broke out again in 1896 and returned again in 1897.

On the whole, the history of these various recent epidemics suggests the possibility that beri-beri may for some reason be spreading, or may exist in hitherto unsuspected localities. There is apparently some condition in asylums that is favourable to the appearance or spread of the disease. Its appearance in so many different institutions of the same kind so far apart suggests this, but at the same time is against any dietetic theory of origin. In Little Rock and at Tuscaloosa malaria was, perhaps somewhat vaguely, suggested as a cause. Bad hygienic conditions, antecedent overcrowding and prevalence of dysentery, pre-existed in the Suffolk Asylum, and were also present in the Dublin Asylum. Though I incline to attribute great importance to these factors in the actual development of the disease, no modern physician will probably recognise that they are in themselves sufficient to produce it. In view of the recent revival of the views connecting beri-beri with rice, the negative evidence of these asylum epidemics is perhaps of some value.

Reference and Note.

[1] *Alg. Zeit. f. Psych.*, Bd. LV, H. I. [2] Dr. Bondurant in his account of the epidemic at Tuscaloosa has drawn attention to the special liability of epileptics to attacks of beri-beri.

10 P.353

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Dr Patrick Manson

THE CLINICAL FEATURES OF BERI-BERI

with the author's compliments

BY

CONOLLY NORMAN, F.R.C.P.I.;
Medical Superintendent, Richmond Asylum, Dublin.

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PREFACE.

In submitting this Paper, reprinted with a few press corrections from the seventeenth volume of the "Transactions of the Royal Academy of Medicine in Ireland," I have to add my acknowledgments to various friends who have aided me in my work on this subject.

My thanks are due to Dr. Walter G. Smith and Sir Thornley Stoker (then respectively Presidents of the Royal College of Physicians of Ireland and of the Royal College of Surgeons in Ireland), who were so kind as to see my cases with me in consultation in the autumn of 1894, and again in 1896. On the latter occasion both gentlemen were good enough to write valuable reports.

I owe much to the kindness of Dr. Patrick Manson, who not only saw my cases in consultation in 1896, but has also given me from the fulness of his knowledge much valuable information and advice many times since then. I am indebted to Dr. Manson for my first acquaintance with the very interesting recent epidemic at Sainte-Gemmes.

The Dutch Government, at my invitation, sent over a couple of naval surgeons, Drs. Verschuur and Eysselsteijn, to study the epidemic of 1897. I have to thank these experienced officers for much useful information most courteously given.

Lastly, I acknowledge with special pleasure my indebtedness to my own colleagues, particularly Drs. Cullinan, Rambaut, and Fleury, for the care with which they followed the cases and for the accuracy of their notes, without which the present compilation would have been impossible. Their observations were often carried out amidst the difficulties arising from overwork and other discouragements, and are, therefore, the more appreciated by me. Drs. Cullinan and Rambaut were so good as to take the photographs, reproductions of which appear at the end of this pamphlet. Dr. Rambaut was also kind enough to procure for me some translations from the Dutch and to permit me to use his rendering (which I hope may soon be published) of Scheube's monograph.

C. N.

THE CLINICAL FEATURES OF BERI-BERI.[a]

Though many interesting observations on the subject of beri-beri have been made public during the last few years, and though two or three learned treatises exist dealing at length with the affection in question, yet the disease retains a peculiar interest on account of its uncertain pathology, its disputed causation, its comparative rarity outside certain well-marked limits, and finally, its characteristically varied and puzzling symptomatology.

With reference to causation, my experience of beri-beri does not support any of the current theories, save the old one which associates this affection with the over-crowding of human beings into limited spaces under unfavourable hygienic conditions. The occurrence of beri-beri in the crowded quarters of Oriental towns, in hospitals and prisons, and in the crowded holds of ships has been often noted. It is difficult to see how over-crowding can act, save as a predisposing agent, but that there is some connection between the two phenomena cannot reasonably be denied. When beri-beri broke out in the Richmond Asylum, Dublin, in the year 1894, the institution had been extremely over-crowded for a great many years. The general sanitary condition of the Asylum was not good, as was shown by the prevalence of dysentery, and other zymotic diseases. The floors rarely admitted of being waxed, and consequently required constant washing, producing a dampness both of the woodwork and of the atmosphere of the rooms, probably not wholesome.[a]

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[a] Read before the Section of Medicine of the Royal Academy of Medicine in Ireland, Friday, January 27, 1899.

With regard to the morbid anatomy of the disease and its supposed bacterial origin, I am sorry not to be in a position to add anything to the observations of former observers. The peripheral nerves of lower extremities, of the heart, and of the diaphragm were found to present parenchymatous change, and in some old standing cases the peripheral portions of the peroneal nerves presented marked interstitial proliferation and fibroid change. The changes did not seem to differ from those occurring in alcoholic neuritis. We endeavoured to make cultures from the blood, and believed at first that we had succeeded in isolating a coccus identical with or similar to that described by Pekelharing, but subsequent trials showed that we were probably wrong. At all events, our results were not constant.

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[a] The question of the dietetic origin of beri-beri receives a chiefly negative answer from our Dublin experience. There was not an excess of farinaceous food in the dietary of the Asylum. Rice was little used—less than in most private households—never, indeed, except as a "medical comfort" (*i.e.*, an extra article of diet given to some person who was sick or toothless). Meat occupied a more prominent place than in most asylum dietaries, being given six days a week—half a pound at dinner. The water supply is that common to the City of Dublin, wherein the Asylum is situated; the water is not stored; it was frequently tested and was always found free from lead or other mineral or organic poison. There was nothing supplied to the patients which is not, as far as I am aware, in common use in the city. One substance had been added to the dietary in the beginning of the year 1894—namely, dried ling, which was given for Friday's dinner. This probably came from Newfoundland, and taken in connection with the existence of beri-beri amongst the fishermen of the Newfoundland Banks, was perhaps open to suspicion. But, apart from the fact that similar dried fish is extensively used by the poor throughout Dublin, two remarkable facts seem to absolve this dried ling. One is that in the wards where beri-beri probably first broke out, and certainly where it most prevailed, fish for certain administrative reasons had not been used at all. Another is that though the use of dried fish was stopped altogether in 1894, and fresh fish from home waters substituted, yet beri-beri returned in 1896 and subsequent years. Of course it is open to anyone who inclines to specially suspect Newfoundland dried fish to say that the substance in question was merely the carrier of the poison producing the disease, and that this poison, once introduced, multiplied according to its own laws, but that line of argument would suggest that Rangoon sugar, Java rice, nay, even frozen beef from Matto Grosso in Brazil, or many other tropical products should carry beri-beri into Europe daily.

The notion that beri-beri is strictly a merely tropical disease may probably now be regarded as exploded. This I have elsewhere shown.[a]

That beri-beri contracted in the tropics can continue for some time in temperate climates is evident from many records.

Lascar and other sailors are not uncommonly landed at English ports affected with this disease, and occasionally die of it in English hospitals. I have seen such cases at the Seamen's Hospital, Albert Dock, through the kindness of Dr. Manson. Within the last few weeks, through the goodness of Dr. Walter G. Smith, I had an opportunity of seeing, in Sir Patrick Dun's Hospital in this city, two cases of beri-beri in the persons of Norwegian sailors whose ships, on the return voyage from Florida with a cargo of timber, had been attacked with beri-beri, which killed the steward and invalided a number of the crew. Manson's cases are well known, which actually broke out in the port of London among a Lascar crew, shut up in the steamy atmosphere of the hold which they never left through fear of the climate. These people probably bring with them the peculiar environment which is favourable to the development of the disease if they do not in any special way carry its poison. So that although it is true that of the many European soldiers who have returned home invalided with this disease it is not recorded that any have served as a focus for the spread of the affection, we still cannot definitely say that this climate is fatal to beri-beri. The records of the disease in Saghalien, above referred to (Grimm), confirm this opinion.

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[a] "Beri-beri Occurring in Temperate Climates," Brit. Med. Journ. Sept. 24, 1898. See also Grimm's Monograph, "Klinische Beobachtungen über Beri-Beri."

It is probably dangerous in the present state of our knowledge to circumscribe too closely the limits of endemic diseases. The history of cholera warns us that diseases can travel far from what may be called their normal habitat, and even sometimes settle permanently in distant lands. By the way, it may be that the appearance of beri-beri in Brazil is another example of the same kind, and it seems not improbable that that country has twice, at long intervals, been invaded by beri-beri, which on the first occasion gradually died out, or became inconspicuous. Now, some years after the second invasion, it would appear to be a permanent settler. It is hardly necessary to say that there is much that is still entirely unknown with regard to the spread and decline of communicable diseases locally. The spread of leprosy throughout Europe about the time of Charlemagne and the gradual process of its extinction, the commencement of which seems to date from the termination of the fifteenth century, have never been explained. The decrease and limitation of the disease cannot have been due to cleanliness, nor to effective isolation, since neither of these was understood in mediæval Europe.

There is then a possibility that beri-beri may be at present spreading or tending to spread in Europe and North America. There are certainly some grounds for thinking that it is specially liable to attack the insane in institutions. It has been suggested that the disease may have existed in these countries, and may have escaped observation among the crowded populations of workhouses, asylums, &c. It is, of course, quite possible—nay, probable—that isolated cases may occur from time to time, and fail to receive recognition, but I do not think it is possible that an extensive outbreak could long be overlooked, especially as this disease, like most similar affections, tends when it breaks out in a new place to appear in its severer forms.

With regard to the clinical phenomena of the disease one or two preliminary remarks seem called for. The insane are unfortunately not favourable persons in whom to observe certain nervous troubles. Pain and anæsthesia, for example, are difficult to pecisely confirm. A large number of the asylum patients attacked were dull epileptics, and chronic dements who could give little reliable account of themselves. The occasional concomitance of beri-beri with paralysis due to some common cause, or with diseases other than cerebral (old heart or lung affections), sometimes aided to render the precise recognition of the morbid signs of beri-beri difficult. It is interesting to note that no alteration of mental symptoms fairly attributable to beri-beri could be made out. The frequency with which we have to deal with cases of alcoholic neuritis has rendered us familiar with the mental aspects of that affection. They were looked for in our cases of beri-beri, and were not found. Neither was any appreciable change observed in the mental state of the sane who were attacked.[a] The fact that the peculiar form of dysnoia which Korsakow has described as polyneuritic insanity,[b] does not occur in beri-beri seems to show that the opinion is justified, which has been held by most observers, of whom I am one—namely, that Korsakow's disease is really dependent upon the action on the cerebral cortex of certain poisons which also produce neuritis, and is not directly connected with neuritis. In a few recent cases of mental disease which were attacked with severe beri-beri which they survived, that amelioration of mental troubles occurred which is often noted as following, in similar cases, the incidence of any severe intercurrent malady. This took place notably in the cases of two acute melancholiacs, attacked in 1894, in both of whom mental accompanied bodily convalescence. One, an attorney's clerk, resumed his calling, which he continues to follow. The other, a militia man, who had altogether lost power of his lower extremities, served through the training of his regiment next year, and when last heard of continued in every way well. Often, of course, this favourable result did not occur. A young woman suffering from acute mania associated with pregnancy and accompanied with great excitement, contracted beri-beri in 1894 with general anasarca and severe heart trouble. While convalescent from beri-beri she was delivered of a living child. No mental improvement followed, and she has since drifted into agitated dementia quite in the ordinary way of uncured cases of mania.

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[a] Ridley (Dublin Hospital Reports, Vol. II., 1818, p. 227) tells us that when he himself suffered from beri-beri his memory became considerably impaired. This impairment of memory was one of the troubles which persisted in his case for a long time, and even after his return home. Scheube, who does not mention mental troubles in his great monograph ("Die Beri-beri Krankheit, 1894"), tells us in the article on beri-beri in his work on "The Diseases of Warm Climates" (1896) that weakness of memory, melancholia, and enlargement of the liver have often been observed as residua after beri-beri.

[b] Korsakow, Archiv. f. Psychiatrie. XXI., 669. Do., do., XXXII., 112. Allg. Zeitschrift f. Psychiatrie. XLVI., 475. Do., do., XLVII., 390. Tiling, Allg. Zeitschrift f. Psych. XLVI., 233. Do., do., XLVIII., 549. Ernst Meyer, Zeitschrift für Psych. LV., 267. S. Kahlbaum, Zeitschrift f. Psych. LVI., 428. Mönkemöller, Zeitschrift f. Psych. LIV., 806. Jolly, Charité-Annalen. XXII. Buccelli, Riv. di Pathologia Nervosa e Mentale. III., 249. Soukhanoff, Revue de Médecine. 1897. No. 5.

Disturbances of sensation, although as might be expected often missing among the insane, are without doubt one of the earliest indications of beri-beri. They were always the first subject of complaint among the sane sufferers at the Dublin asylum. A painful sense of weariness and weight was one of the first troubles. The patient felt tired as to his legs after slight exertion or towards evening. He experienced a sensation as if the limbs were heavy. As these conditions increased they were usually accompanied by a dull aching in the calves. Later on this aching sometimes became a prominent symptom, the pain being evidently very severe. At first, however, there was commonly no great continuous muscular pain. Cramps in the calf muscles, chiefly at night, were of early occurrence, and very often formed the immediate reason of the patient reporting himself ill. He then mentioned the weary feelings which he had perhaps experienced for some days, but which had not till now seemed to him of much consequence. The cardiac and dropsical signs may have already appeared, but not in a manner to attract the patient's notice. Numbness as a spontaneous sensation was often experienced; or numbness became evident when the patient touched anything with his foot, or in some cases with his hand. One of my head nurses, a woman of intelligence and observation, noticed amongst her earliest troubles that when she tried to ride her bicycle she could not feel the pedals with her soles, and when she wrote she could not distinctly feel her pen with her fingers.

Muscular pains, cramps, aching pains, and more rarely pains shooting down the legs, were accompanied by pains of a boring or stinging or burning character, the seat of which appeared to be chiefly in the skin. A very common complaint was that the patient felt as if stung with nettles. Occasionally special and severe pain was complained of in the soles of the feet; this was usually likened to burning. One patient said he felt as if his feet were plunged in hot lime.

The most frequent spontaneous complaint, when the disease was fully developed, and probably the most characteristic, was of a sensation as if something was creeping over a blistered surface. This feeling (painful formication) to which the Japanese observers have drawn special attention under the name of *piri-piri*, probably belongs to the mixed order of combined hypo and hyperæsthesiæ. A certain degree of anæsthesia or hypoæsthesia, perhaps arising from a change affecting special superficially distributed filaments, produces the feeling as if the skin had been deadened or removed; while hyperæsthesia resulting from a change affecting other filaments brings about a sensation of tickling, smarting, and tingling compared to the creeping of insects, or the stinging of ants. However conditioned, this *piri-piri* is often a state of great suffering. It was extremely well marked in one of my nurses who suffered intensely from it, particularly at night.

In searching for tenderness and anæsthesia, not spontaneously complained of, some care is necessary, as a variety of conditions are found which might deceive a careless observer. The superficial nerves were always tender where sensibility could be judged at all. This was specially the case with the peroneal nerve. The saphenus in the lower third of the inside of the thigh was also very frequently tender. The calf muscles were tender on pressure. Together with this tenderness to deep pressure there were varying degrees of superficial anæsthesia or hypoæsthesia. The latter conditions were, of course, less easy to confirm in the insane than the former. A firm grasping of the calf so as to produce pressure on the muscles nearly always caused marked wincing, whereas it was often impossible, owing to the patient's mental state, to be sure as to the existence of diminution of superficial sensibility. Nevertheless, from its invariable presence in the sane sufferers and from the frequency with which it could be demonstrated in the more intelligent among the insane, I have little doubt that it always existed. It was very variable in extent and degree. It was usually associated with conditions of paræsthesia (sensations of formication and the like). Very often we found that the patient who was insensible to light pressure (the drawing of a pencil or feather lightly over the skin) complained of pain of a formicating character when the pencil was drawn more firmly over the same area. Slighter forms of hypoæsthesia could be demonstrated by the patient's inability to distinguish whether he was being touched by a naked or gloved finger, also to recognise when a piece of stout paper was placed between his skin and the finger which touched him. The æsthesiometer was often used to demonstrate great enlargement of the tactile areas, but, on the whole, this instrument requires too much patience and intelligence on the part of the patient to be of much service. The muscular sense and the sense of temperature, so far as they could be judged, did not appear specially engaged. In the experiment mentioned above with glove and paper a keen sense would have recognised a difference between the temperature of those objects and of the finger.

A phenomenon was frequently observed among my patients which I have not found elsewhere recorded in descriptions of beri-beri—namely, the occurrence round each zone of hypoæsthesia of a very distinct zone of hyperæsthesia. Thus when the pencil passed from the region where light pressure could not be perceived, the same degree of pressure caused immediate wincing before a region was reached where sensation seemed normal, showing that the zones where sensation was lowered were bordered by tracts of tenderness.

In some cases there was very marked painful anæsthesia. The patient complained of numbness, could not appreciate the duality of two touching points, could not recognise touching objects, and yet the least touch caused pain.

Patches of cutaneous hyperæsthesia, anæsthesia, hypoæsthesia, or paræsthesia were found in various parts of the body. In some cases alteration in cutaneous sensibility was probably almost general. More often it occurred in limited patches, sometimes corresponding to the distribution of certain cutaneous nerves, often apparently quite without such correspondence. Hypoæsthesia, with more or less paræsthesia, occurring over the legs from knee to ankle in irregular tracts, and similarly on dorsum of foot was the sensory phenomenon which was actually most commonly demonstrated (next to the practically universal tenderness of the calf muscles). Sensory troubles, whether deep or superficial, seemed always to begin in the legs. Tracts of anæsthesia were found also on the thighs, on the trunk,[a] on the upper extremities, on the nucha, and on the face. Two patients—a nurse and a lunatic—presented isolated patches of anæsthesia about the lips. One nurse presented anæsthesia of the face, at first strictly unilateral and later extending towards the opposite side in the region about the mouth. It has been said that there is a special tendency in beri-beri for the sensation of the superficial tissues round the mouth to be engaged.[b] In the case of the nurse above referred to this engagement involved the red border of the lips, and the patient complained that she could not properly feel her cup when she drank. Anæsthetic patches and tracts sometimes lasted for a considerable time; sometimes with little change; sometimes spreading gradually and gradually diminishing. On the other hand, when carefully watched and traced, they were very frequently found to vary, little or much, from day to day; sometimes they vanished with singular suddenness. The painful formication was often worse at night. On the contrary, anæsthetic patches were sometimes found to be present in the morning, and to disappear in the evening. It has been suggested that this fugacious anæsthesia is unlike that of the Eastern beri-beri, but this observation of anæsthesia present in the morning and disappearing in the evening has been recorded by Scheube in his great monograph on beri-beri, as seen by him in Japan. When this particular phenomenon was first noticed in the Dublin Asylum by one of my assistants, who was not then acquainted with Scheube's observation, the conclusion was arrived at by that officer that there had been an error in recording the diminished sensation, but the correctness of the observation was confirmed by myself in the same and in some other cases.[a]

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[a] Including back and front of chest, sides, abdomen, and loins. Scheube observes that in his experience the back remains free. In one of my cases, patches of hypoæsthesia with paræsthesia were very well marked on the loins, lateral aspects of chest, and in the scapular and intra-scapular regions.

[b] Observed as long ago as the time of Ridley (loc. cit.), emphasised by Scheube, and rightly stated by him to occur in some cases where hypoæsthesia is not widespread. Pekelharing and Winkler state that they have not met this condition.

Drs. Verschuur and Eysselsteijn having pointed out to me, what I had not before noticed, that some of my cases presented anæsthesia of the pharynx—a condition which they informed me is common in Javanese beri-beri—we searched for this phenomenon, and found it in most cases in which examination could be satisfactorily carried out.[b]

With regard to the condition of the reflexes, my observation coincides with those of Grimm, who emphasises the fact that so far from the abolition of the knee-jerks being a prominent feature of the disease in all stages, the knee-jerk is exaggerated, as are all the reflexes, superficial and deep, in the earlier stages. In one of my patients (a nurse in the early period of the disease) I obtained by the artifice of pressing down the patella with the left index, as the patient lay in bed with legs extended, and then striking the left index with the right finger tips—a double reaction:—first a jerk without appreciable interval, probably representing myotatic excitability; and secondly, a stronger jerk succeeding after a distinct interval, and being no doubt a superficial reflex which was exaggerated because the whole lower limb was hyperæsthetic. The knee-jerk can rarely be produced by this manœuvre in normal individuals. As cases progressed the knee-jerks were usually diminished. sometimes unequally on the two sides. When there was complete loss of power they were abolished. Many cases in the first epidemic were undoubtedly not discovered in the early stage, and hence abolition of knee-jerk was then more often noted than subsequently. The circumstance that cases often do not come under notice in the first stage has, no doubt, given rise to the prevailing idea as to the knee-jerks being uniformly absent.[a]

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[a] When this paper was read Dr. Littledale stated that he had independently noticed this particular condition in the Norwegian sailors suffering from beri-beri in Sir Patrick Dun's Hospital. A curious and interesting confirmation is thus afforded of the accuracy of Scheube's observation, whom almost nothing seems to have escaped.

[b] It is to be observed that one of Ridley's patients (loc. cit.) "complained of an internal sensation of great heat, particularly in expiration, when he observed 'that his breath burned his throat.'" This condition was probably due to hyperæsthesia or paræsthesia of the larynx or pharynx.

The motor like the sensory engagement was variable. The earliest symptom was a slight affection of the peroneal muscles and the flexors of the foot. In consequence the foot tended to drop and become inverted. In slighter cases this tendency showed itself in the posture of the limbs when the patient was at rest the foot being over-extended and falling inwards, yet by an effort of will the patient could rectify the condition, and the gait was little or not at all engaged. In most cases, however, the power of walking was impaired. Some patients progressed in a hobbling, swaying fashion which they attributed to pain or to general weakness of the lower extremities. The most characteristic peculiarity of gait, and the most frequent, was an approximation more or less complete to the condition described by Charcot[a] as steppage, or the gait of the stepper (high stepping horse). Here, as in similar conditions, the high action was evidently due to the difficulty of getting the drooping foot clear of the ground. This caused the knee to be raised too high, and the movement being unrestrained by the tone of the leg muscles this elevation of the knee was accomplished with a jerk. The foot was then precipitated forwards something after the fashion of the tabetic, but with this difference, that instead of the heel striking the ground first, as the foot was flopped down, the drooping toes struck first and afterwards the heel. As the patient walked bare-foot across the floor, the double impact was very evident both to the eye and ear (pseudo-tabes of Blocq).[b] The patient leaned forward in walking, and when he clumsily brought his leg to the stationary point, it swayed under him. His tendency was to fall forwards, if unsupported. The maintenance of the static posture was difficult. This was partly owing to the relaxed condition of the knee-joint which wobbled with a tendency to too free backward movement, and partly to general enfeeblement of the extensors. The patient in endeavouring to support himself constantly changed his *point d'appui* from one foot to another, producing the "equilibrium of the velocipedist" of M. Grasset. All these conditions correspond to the well ascertained indications of peripheral neuritis, and may be found in the ordinary alcoholic variety. In a few of our cases of beri-beri they were presented in an exquisite form and under circumstances which rendered their study possible. In others the exact state described was more or less complicated, or in its typical form was transitory, being soon followed by increased paralysis which rendered walking impossible. In one case there was the characteristic steppage in one leg, while in the other a slight degree of lateral dragging of the whole extremity was added, producing a resemblance to the hemiplegic type. The muscles of the thigh were often paralysed. Here, as elsewhere, the extensors were first and chiefly affected. The degree of engagement was very variable. Some patients were unable to extend the knee even when lying in bed in a lateral posture. Others, though unable to walk, were able to stand so long as they could be kept in a perfectly upright attitude, but so soon as the knees were bent in the least they collapsed, owing to feebleness of the quadriceps extensor femoris. Many patients could not rise from the sitting posture without help. Some restless and maniacal, being unable to walk or stand, progressed by sitting on the floor and helping themselves along by their hands placed behind them. Some patients, made to sit up on the edge of their beds with their feet out, used to help themselves back into the supine position by leaning on their hands and swinging their hips round so as to get their legs into bed without any movement of the thigh muscles.

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[a] Pekelharing and Winkler have noted that the knee-jerk may be much increased at the commencement of the illness, and that there may be ankle clonus. Scheube tells that in one epidemic observed by him in 1880. knee-jerk was absent in 37 per cent. of the cases; in another, in 1881, it was absent in 48 per cent.

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[a] Charcot. Clinique des Maladies du Système Nerveux. Guinon. P. 270.

[b] Diagnostic des affections qui ont été rapprochées cliniquement du tabes. Blocq. Gazette des Hôpitaux. 1890. No. 35.

The trunk muscles were seldom markedly engaged, but some patients had difficulty in raising the body in bed or in sitting up, and occasionally some feebleness was noticeable in raising the head. In several patients a somewhat pendulous condition of the abdomen, probably due to impairment of the abdominal muscles, was noticeable. It will be remembered that the constipation commonly observed in beri-beri has been attributed in part to want of power in the abdominal muscles, and Miura (quoted by Scheube) even believed that he was able to demonstrate in one case paralysis of the levator ani.

The upper extremities were much less frequently engaged than the lower. Contrary to the habit of lead, the beri-beri poison attacks preferentially the nerves of the lower extremities. In the cases at the Richmond Asylum the engagement of the upper extremities seems to have been even less than usual, but there may be an element of error here, owing to the absence of complaint in many of our people and the difficulty of testing (especially in those who do not assist one) the slighter forms of paralysis in the arms compared with the readiness with which alterations in the gait can be observed. In something less than 1 per cent. of all our cases there was actual drop wrist, and in one case this condition was extreme. In others the power of extension was impaired, and there was marked tenderness of the arm muscles.

General muscular feebleness was not uncommon, showing itself by indisposition for exertion of any kind, inability to maintain any posture of strain, and a tendency of the limbs to assume whatever position gravitation favoured. In a few extreme cases this condition passed on into a state of universal paresis, in which the patient seemed to have little power of voluntary movement of any kind.

Professor Anderson having pointed out to me that the muscles of mastication are often enfeebled in beri-beri, I made a few experiments by giving patients nuts to crack with their teeth, but obtained no satisfactory evidence of loss of power. This may have existed in many severe cases which were not tested, or in many of the earlier cases.

In one case ptosis, external strabismus, and dilatation of the pupil occurred unilaterally. Engagement of the third nerve is a rare condition in beri-beri. Scheube does not mention its occurrence, but says he saw one case of ocular palsy affecting the external rectus, and quotes Da Silva Lima as having seen in rare cases strabismus and double vision.

On the other hand, facial paralysis, single or double, difficulty of swallowing, difficult movements of the tongue, and disturbance of articulation were not observed.

The sphincters were never paralysed in our cases.

The paralytic phenomena were not infrequently much more marked on one side than on the other. This irregularity has been observed by Scheube, who has also noted that the arm of one side and the leg of the other may be chiefly affected. This observer has also seen the paralysis confined entirely to one side, and he tells of a case in which, throughout three attacks, only the left leg was affected.

It may be mentioned that in some of our cases the sensory and dropsical phenomena like the motor showed a marked preference for one side.

The affected muscles in the earlier stage often presented a peculiar hardness to pressure. This seemed sometimes pretty uniform; more often, however, the muscular mass presented irregularities as if containing hard lumps lying in the long axis of the muscle. This was specially noted in the inner portion of the gastrocnemius (Anderson and Scheube).

As the cases progressed, atrophy of the affected muscles set in. The muscles then became wasted, soft, and flabby. *Post-mortem* their changed appearance was manifest to the naked eye, a yellowish colour taking the place of the natural colour of flesh. Degrees of change in the fibres were seen under the microscope varying from mere loss of striation to marked granular or fatty degeneration. This atrophy of the muscles is the cause of the wasting which occurs in the so-called "dry" form of beri-beri. The disease, as my hearers are aware, has been divided by the earlier observers into two forms, the "wet" and the "dry"—meaning cases in which respectively dropsy and atrophy are predominating features. The division is very artificial and imperfect, for there is no real distinction, and a "wet" case may be found profoundly atrophic when the dropsy subsides and permits of a proper examination of the muscles. On the other hand we certainly had cases in which atrophy and paralysis appeared without dropsy having been noticed, but, considering the peculiarities of our population, and the fact that in many cases the preliminary œdema was very fugacious, I am disposed to think that œdema was always present and was sometimes overlooked, so that our atrophic cases were not truly "dry" in the sense of never having suffered from œdema.

Contractures of the lower extremities, which, though rare, are not unknown in beri-beri (Simmons, Bälz, Scheube), occurred in five of our cases. Scheube dwells upon the long and tedious nature of this condition, and tells us that in many cases it is never perfectly recovered from. Nevertheless, only two of our people remain permanently crippled from this cause, and, taking into account the difficulty of managing the insane, I think one can neither wonder at the occurrence of these contractures nor at the failure to rectify them in a few cases; for, though Scheube holds that they do not arise merely from the predominance of the flexor muscles in the long condition of inactivity imposed upon the patient, yet everyone who has much to do with the insane knows how often contractures tend to occur in lunatics who are bed-ridden from any cause, even where there is no specific ailment of nerve and muscle.

A very remarkable condition of relaxation of the joints of the affected extremities was usually observed. Manson mentions the condition in his monograph in Davidson's "Diseases of Warm Climates," but does not dwell upon it, and I have not been able to find it referred to elsewhere in connection with beri-beri. It is nevertheless very striking. When a patient thus affected stands the knees bend in a hyperextended position to a degree quite impossible in health, and which I have not seen save in the joint affection of tabes dorsalis. The arch of the foot is lowered, and a condition of flat foot is produced which is sometimes extreme. Again, if the patient is made to lie on his face and the knees are flexed, the heel can be readily made to touch the buttock on each side, the condition of the knee-joint becoming one of sub-luxation. Similarly the ankle-joint admitted of a degree of movement quite abnormal. In many cases if one grasped the shin and shook the limb, the foot swung about with a flail-like movement. In patients lying on the face with the heels resting on the buttocks, the feet fell inwards as though the anterior ligaments of the ankle-joints had been divided. I found this condition not only in patients in whom there was marked wasting of the muscles, but also in persons whose muscles were still plump, and whose gait was little or scarcely at all affected. I therefore think it is characteristic of the disease. Whether it is sufficiently accounted for by supposing that it is due to mere loss of support dependent on deficient muscular power I do not take upon myself to say; but having seen, a few years ago, a very extreme condition similar to this, occurring in connection with the knee-joint, in a case of tabetic general paralysis in which the bones had not undergone the changes common in Charcot's joint disease, I am inclined to think that there may be some specific trophic condition in diseases affecting the peripheral nerves, or the sensory neurons, whereby the ligamentous structures become altered. It is not due in beri-beri solely to wasting of muscles, nor does it only occur in persons long confined to bed. I demonstrated this condition in Lascar sailors whom I saw, through Dr. Manson's kindness in his wards at the Royal Albert Hospital, and in Dr. Smith's patients at Sir Patrick Dun's Hospital (see p. 5). The latter were Norwegian sailors—one elderly, the other young, both evidently strong men before the oncome of beri-beri. Neither the Lascars nor the Norwegians had been long confined to bed.

Cardiac trouble is one of the most constant conditions in beri-beri. Palpitations occurred in 60 per cent. of Anderson's cases and Scheube remarks that it is one of the most frequent subjects of complaint. All my sane patients complained either of palpitation or sense of oppression about the heart; very often of both. In one nurse palpitation was sufficiently severe and persistent to be alone a frequent cause of insomnia. On the whole, however, I would say that tachycardia and irritability of the heart are more characteristic than palpitation. Tachycardia was, I think, invariable in our cases. It was often very well-marked when other signs were not advanced. Thus a patient while lying quietly in bed would have a pulse of 100, 112, or 120, while there was no apparent distress and little sensory or motor trouble, and when dropsy could only be detected by careful examination. Even more remarkable than the rapidity of the pulse was its irritability. The least exertion was commonly followed by a singular increase of pulse rate. A patient's pulse while he lay down was 100; when he sat up it rose to 120; when he walked 20 feet it rose to 140 or 160 or higher. The acceleration which followed even the slightest exertion was very alarming, and in observing maniacal cases, in which protracted restlessness was accompanied by a pulse too fast to be counted, alarm gave place to wonder. Spontaneous variation in the pulse rate—that is, variation occurring while the patient remained in the same posture and depending on no apparent cause—was common. A curious condition which has before been noted in beri-beri, but which has not, as far as I know, received any particular name, was so common and characteristic as to deserve a special appellation. I have, therefore, proposed to call it unconformability. In this state the heart's impulse and the pulse do not correspond. The heart is acting with apparent vigour; the impulse is perhaps very distinctly visible, at any rate feels forcible to the hand laid upon the chest; the sounds are loud and the impulse conveyed by the stethoscope is strong. Yet the pulse is small, maybe extremely small, sometimes little more than perceptible. It was not uncommonly found that the pulse counted at the wrist did not correspond to the heart, some beats being apparently altogether lost or a beat being registered by the sphygmograph which was too feeble to be felt with the finger. This unconformability varies in different cases and in different stages of the same case, but it is very generally present, and one soon learns to recognise it as a prominent feature in the disease. Action of the heart, so violent as to shake the whole chest and to be noticeable as soon as one saw the patient, occurred in some cases. This condition was common in the first epidemic and in cases which terminated unfavourably. In milder cases and in the later epidemics it was by no means prominent. However, even there violent heaving action could be produced in some cases, by making the patient undergo any exertion, though it had not been evident when he was at rest.

The area of cardiac dulness was often increased, particularly towards the right. The singular phenomenon, observed in beri-beri, of a sudden increase in the area of cardiac dulness was confirmed in several of our cases.

Auscultatory signs varied. In some the normal order of the sounds was replaced by what Manson has called a pendulum sound, the sound of the tic-tac of a clock, the first and second sounds not having the ordinary relation to each other, but being about the same length, and each pair of sounds being separated from the rest by an interval of about the same length as that between the individual sounds. In many cases this tic-tac arrangement could be produced by slight exertion. Spontaneous variation of the rate and rhythm of the sounds occurred A very common condition was accentuation of the second pulmonary sound. Reduplication of the second sound was common, producing a triple rhythm. This was most generally audible at the apex. Occasionally reduplication or "splitting" of the first sound appeared. Sometimes *bruits* were audible, mostly in the form of a soft blowing murmur with the first sound over the pulmonary area, less often at apex. These murmurs were variable and inconstant, and sometimes were only audible after exertion. Precordial anxiety was common even in slight cases, and the sense of weight and oppression about the heart was often distressing In severe cases orthopnœa and urgent cardiac distress often ushered in the end.

Post mortem, varying degrees of dilatation especially of the right side of the heart, with or without hypertrophy, were found in acute cases. In almost all cases there was marked evidence of fatty degeneration of the heart muscle.

Respiration was usually quickened, and was often accompanied with oppression, even when there was not œdema pulmonum. In a few cases a sense of weight and constriction was complained of, somewhat like a girdle pain. These sensations may have been due to impairment of the respiratory muscles, intercostals and diaphragm. The respiration was in some cases thoracic from feebleness of the diaphragm. In several cases paralysis of the muscles of respiration obviously contributed to the end. Sometimes, even in cases which terminated favourably, there was for some time an inability to cough deeply or to sneeze.

Impairment or even loss of voice occurred in a few cases. In one or two cases sudden death may have been due to laryngeal paralysis, but this was not proved.

A feeling of weight and discomfort in the stomach was not an infrequent complaint. The appetite was often unimpaired, even in cases of some gravity. Some of the insane ate greedily and had to be restrained from doing so as they produced sickness of stomach by over-feeding. Vomiting occurred in about 5 per cent. of all our cases. In 1894 it occurred chiefly towards the end in unfavourable cases, and this is the experience of the Japanese physicians and others, so that vomiting has come to be considered a malum signum. It is probable that different epidemics differ somewhat in this as in other particulars.[a] In our later epidemics, vomiting had not the bad significance which it had in the first A few cases were preceded by vomiting and sometimes also by diarrhœa. The latter, however, was rare. Generally there was a tendency to constipation throughout, especially in cases in which there was much anasarca.

In a few cases albumen was found in the urine, usually merely a trace, and generally only as a transient phenomenon. The urine was apt to be scanty and concentrated in cases where dropsy was pronounced.

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[a] Ridley, writing from his experiences in Ceylon, says, "the irritability of the stomach is frequently so great as to preclude the use of medicine by the mouth." Evidently vomiting was common among his patients, and had no specially bad prognostic significance. In the epidemic at Sainte-Gemmes-sur-Loire, to be presently referred to, vomiting and diarrhœa were common prodromata.

Œdema is one of the leading signs of beri-beri. I believe it is always present. It is sometimes slight, transitory and easily overlooked. It is perhaps correct to say, as is generally said, and as I am in the habit of saying, that it begins in the pretibial region. It is usually easily demonstrated there in early stages of the disease and in mild cases. Unlike the œdema of cardiac or renal disease it does not begin about the ankles, which are often quite unaffected, but appears along the inner side of the tibia. This peculiarity has been noted by Pekelharing and Winkler, who describe the pear-shaped swelling resulting from the peculiar situation of the œdema. Slight œdema I have found could generally be detected early over the sacrum, frequently also over the sternum or ribs and over the ulnar border of the forearm. Not seldom, even in mild cases, and where one could not say that there was general anasarca, the face was notably puffy. Sometimes the feet and legs generally became œdematous. Some cases presented general anasarca, often extreme. The dropsy of the superficial tissues presented certain peculiarities. The degree of œdema in different parts of the body seemed to vary spontaneously—that is, without any assignable cause. Thus, one day the right side would be much more water-logged than the left, next day the condition would be reversed. Also the œdema seemed to shift with altered position more rapidly and markedly than is common in other dropsical states. It also disappeared sometimes with a rapidity unknown in other affections. The foregoing remarks chiefly apply to the marked cases of anasarca with deep pitting, which were common when the disease first appeared and less frequent in the later epidemics. It has been said that the œdema in beri-beri is more doughy than inclined to pit, that it is somewhere midway between the ordinary forms of dropsical swelling and a condition of myxœdema. This is the state found in Brazil, as I am informed by a friend who has seen beri-beri there. This is the state which I found among the beri-beri patients in the Suffolk Asylum in 1895, This state is also described by the recorders of the epidemic at Sainte-Gemmes-sur-Loire. This state did not prevail at the Richmond in 1894, but it was the more general form in which œdema appeared in the epidemics of 1896 and the subsequent years. It is particularly apt to occur in recurrent and chronic cases.

Œdema of the deeper structures was often the cause of death. Œdema of the lungs was common. Hydropleura was pretty constant in fatal cases and hydropericardium common. Occasionally a small quantity of effusion into the peritoneum was observed. The joints exhibited occasionally slight effusion especially the knee. Dr. Swanzy examined the fundus oculi in some cases and found the existence of œdema. *Post-mortem,* œdema of the cerebral pia-arachnoid was often marked.

I did not find electrical reactions of the service which I had hoped from the observations of Pekelharing and Winkler. This may have been in part due to the difficulty which most of my patients presented to such tests, in part to my own regrettable want of familiarity with this particular class of investigations. In some cases I could detect no electrical changes. There were many in which the changes were small. In several no abnormality was discovered except that the contractions were slow to galvanic stimulation, and the latent period long, the changes being only of a quantitative nature. Where there was marked atrophy of the muscles, reaction of degeneration was found. The electrical alterations seemed to disappear early in convalescence, and in this our observations confirm those of Zwardemaaker and Kraft who have noted that the heart symptoms may long survive the electrical changes.

It may be well to summarise the clinical appearances and briefly refer to the general course of the cases.[a] The

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[a] In reading this paper I did not dwell upon the history of the various epidemics at the Richmond Asylum which was tolerably familiar to my audience. For others it is necessary to add the following:—

"*History of the Several Epidemics.*—The first epidemic occurred in 1894. The precise period of its outbreak is doubtful. I am sure that at first many mild cases were overlooked and many cases were misunderstood. I may perhaps be pardoned for pointing out that similar mistakes occur among those who first see beri-beri even in its recognised habitats and in a sane population." (At any rate they occurred with me.) "In the year 1894, the average daily number of patients resident in the asylum was 1,503. During the year 174 cases of beri-beri were registered; of these, 127 were male and 47 female patients. No members of the staff (sane persons) were attacked in 1894. The monthly distribution of the occurring cases showed that they increased, gradually at first and then more rapidly, from June to September, and then decreased rapidly in October, after which month no fresh cases occurred. Eighteen male and seven female patients were registered as dying from this cause. I believe that, for a reason suggested above, all these figures represent a considerable underestimate. Taking the figures as they stand, however, they show that 14·3 per cent. of those attacked died. No fresh cases occurred during the year 1895.

"In the year 1896 the daily average number of patients residents was 1,686. Beri-beri reappeared in July, and increased till September. Cases continued to occur until the end of the year. The total number attacked was 114, being 31 male and 76 female patients, with 7 (sane) nurses. Two male and 6 female patients (about 7 per cent. of those attacked) died. None of the nurses died.

"In 1897, with an average insane population of 1,800, there occurred 246 cases, 47 male and 199 female. Among these were 2 male attendants and 6 nurses (8 of the sane staff). None of the staff died. The deaths numbered 11, 3 males and 8 females (4·4 per cent. of those attacked). Four cases, which ought properly to be reckoned in the previous epidemic, occurred in January; then none occurred till June, 134 occurred in July, 50 in August, 7 in September, 3 in October, 37 in November, and 6 in December. The three epidemics show a total of 534 recorded cases, with 44 deaths (equal to 8·23 per cent.).

"The following remarks must be made: (1) It must not be forgotten that the record of 1894 is an under estimate. (2) The epidemic of 1896, extended into the following year, and would perhaps better be described as beginning in the July of 1896, and ending in the February of 1897. (3) The epidemic of 1894 attacked more males than females, as is usual with beri-beri. This proportion was reversed in the following epidemics.

"There were remarkable differences between the three epidemics. In the affection occurred principally among the insane, solely among them at first. It was, therefore, perhaps more than usually insidious in its mode of oncome. In the sane weariness in the legs with occasional cramps and breathlessness on slight exertion often preceded more definite signs for some time. Sometimes a smart rise of temperature ushered in the earlier symptoms, but this was by no means invariable, and in any case soon subsided. Grimm insists upon the frequency of this initial fever in beri-beri. Several of our patients took ill just after recovery from dysentery. Two cases commenced while the sufferers were convalescent from typhoid fever. Grimm speaks of similar cases. The disease, once started, was extremely variable in course. Some cases never passed beyond the mildest type of the abortive form (rudimentary form of Scheube). Many such cases were undoubtedly overlooked at first among an asylum population, while in later years, when they were carefully looked for, they went to swell the numbers of

first there was high mortality, *shiyo-shin* was common, there were a large number of cases of general, well-marked œdema, and motor paralysis was pronounced. In the second mortality was lower, *shiyo-shin* rare, general anasarca, though it occurred, was infrequent, and motor troubles were less marked. In the third the great majority of the cases were of that mild type which Scheube calls rudimentary; general anasarca scarcely occurred; loss of power of walking was very rare; but there was a quite special tendency to the occurrence of painful formication *(piri-piri)*: yet in each of the latter epidemics there were cases—often cases of relapse—which recalled the conditions prevalent in the first. It has often been observed how much various epidemics of beri-beri differ from each other. Mortality appears to range from 2·5 per cent. (Bälz) to 74·5 per cent. (Da Silva Lima). It has often been noted that the first epidemic at any given place is the worst, and that as the disease tends to become endemic it grows milder."—"Beri-beri Occurring in Temperate Climates." Brit. Med. Journal, September 24, 1898.

In 1898, 13 fresh cases occurred among the female population. They were all of the rudimentary type. A number of cases hang over from 1896 and subsequent years, cases in which œdema of the legs, impairment of sensation, and tachycardia recur from time to time, especially in the summer. Mere rest in bed produces a subsidence of these conditions which are apt again to reappear when the patient is gotten up.

those affected. In such cases there was often nothing more than disinclination for walking with weariness on slight exertion, slight and often transient œdema in the pretibial region, tenderness of calf muscles with impairment of cutaneous sensation in the leg (not always to be confirmed in the insane), and some degree of tachycardia. Occasionally in such cases the degree of cardiac trouble was much in excess of the other morbid conditions, and some patients whose illness seemed trifling died suddenly, This specially occurred in the old, and in persons who had been debilitated by previous illnesses. Sometimes the course which the case ran was pretty uniform, more frequently it was very irregular. Cases which had begun mildly and had progressed favourably, often apparently merely showing the rudimentary type of the disease, suddenly became unfavourable and rapidly developed the worst symptoms. We had frequently the same experiences elsewhere described by those who have to deal with beri-beri—sudden changes for the worse in cases seemingly doing well; great frequency of relapse; occasional sudden death occurring when convalescence was believed to be progressing favourably. In connection with relapse, and also with sudden death, I may say that when we were first dealing with beri-beri I am sure harm was done by not recognising the necessity for prolonged rest in the recumbent posture. Cases were gotten up too soon. Greater caution in this respect lessened the number of relapses and I think of deaths in the later epidemics. The duration of the disease was entirely uncertain. On the whole, the severer forms seemed to tend to terminate more quickly, whether by recovery or death, than the milder. In cases which did not maintain throughout the rudimentary type, or in such cases when they relapsed, or in cases beginning acutely, there was a general tendency for the œdema, at first only perceptible along the front of the shin, or in a few isolated places to spread, sometimes with great rapidity, while diminution of sensation and loss of power spread or increased concurrently. Then the dropsy abated, leaving the patient still paralysed and extremely wasted. In favourable cases paralysis and anæsthesia then gradually passed off. Alarm and distress often arose from the condition of the heart, and this organ was, as has been said, often affected disproportionately to the other symptoms. Some patients becoming more and more water-logged, or some in whom anasarca was not extreme, showed often quite suddenly extreme dyspnœa with inability to lie down, became dusky or leaden or cyanosed, exhibited violently throbbing carotids and a dilated heart, whose pulsations shook the whole chest, while a flickering pulse was hardly perceptible at the wrist. A sensation of suffocation, an intolerable feeling of oppression about the heart, gave rise to intense suffering. This condition, as has been said, sometimes set in with fulminating rapidity. It was usually ushered in by vomiting, a circumstance which has made the latter symptom of such bad omen in beri-beri. The Japanese know this state under the name of "shiyo-shin," and say that it is never recovered from. The best description of it in English is given by Anderson, who recommends relief by bleeding, and even goes so far as to suggest aspiration of the right side of the heart. The condition is obviously due principally to the failure of a weakened and probably degenerated heart to carry out the extra work thrown upon it. This is accentuated in some cases by effusion into the pericardium, by œdema of the lungs, and by impairment of the diaphragm and other respiratory muscles. Exclusive of shiyo-shin, death often appeared to be due to œdema of the lungs. Hydropleura and hydropericardium were at least contributing agents in some of our cases. Paralysis of the respiratory muscles, particularly the diaphragm, was sometimes responsible for death. Some patients seemed to die slowly of mere general exhaustion, but in these fatty degeneration of heart muscle was usually found. Some beri-beri patients readily succumbed to intercurrent affections. In the epidemic of 1894, quite a disproportionate number of epileptic lunatics were attacked by beri-beri. This at the time I inclined to attribute to certain special unfavourable conditions existing in the epileptic wards (particularly overcrowding, &c.), but in this I was wrong, as I now believe, for the special tendency of beri-beri to attack epileptic patients has since then been noted elsewhere (Tuscaloosa and Sainte-Gemmes). Epileptic sufferers very often died in the status or immediately after a fit. Considering the strain which epileptic seizures throw upon the heart one cannot wonder at this.

Sudden death from syncope occurred in some cases, and occasionally in cases of patients who were apparently progressing to a favourable convalescence. In one such case little could be found in the heart muscle to account for the occurrence of death.

The great danger always present in beri-beri is sudden heart failure. Now how this comes about is, I think, intelligible enough if we consider the other symptoms in connection with their recognised cause. In beri-beri we find degeneration of the peripheral nerves, and we find losses of power and of sensation which we can quite definitely associate with such degeneration. Some of these latter symptoms (anæsthesia, &c.) come and go with remarkable rapidity. They disappear with such suddenness in some cases (see above) that we can scarcely suppose an alteration could be detected in the nerves engaged. But if the nerve involved instead of subserving the function of sensation in the skin of the leg or the integument round the mouth had to do with the movements of the heart or with its nutrition, it is evident that the gravest consequences might follow from what elsewhere would be a mere temporary derangement of function. Or, to look at the matter from another point of view:—there is a form of peripheral palsy with which we are all familiar. When a man dozes in a railway carriage and through pressure on the sciatic trunk his leg "falls asleep," we have a tolerably close reproduction of what we find in beri-beri. We have the same combination of anæsthetic and hyperæsthetic conditions. Normal sensation is abolished, but paræsthesia and painful anæsthesia are very marked. Muscular power is diminished or abolished, and attempted movement gives rise to sharp pain. Even the inability to lean upon the extremity, owing to complete relaxation of the knee-joint, is reproduced. We know the cause of this pressure neurosis. We know that it is an entirely temporary condition, but if we can imagine a similar condition, equally temporary or trivial in its essential nature, occurring in the pneumogastric nerve, we see clearly that the death of the individual would result, and this because the functions of the pneumogastric nerve are such as do not admit of temporary suspension.

Reference has been made to the occurrence of beri-beri in other asylums. An epidemic broke out in the asylum at Tuscaloosa, Alabama, U.S., in the beginning of 1895, and recurred in the early autumn of 1896.[a] There were altogether 71 cases of beri-beri, and 21 deaths. The epileptics suffered most severely. Some cases began suddenly with fever and gastro-intestinal trouble, some very insidiously. The symptoms and the *post-mortem* appearances leave no doubt as to the nature of the disease. A similar outbreak appears to have occurred at the Arkansas Asylum, Little Rock, Arkansas, U.S.A., towards the end of 1895.

An epidemic of beri-beri broke out in the Suffolk County Asylum, Melton, Suffolk, towards the close of 1894. I saw some of the cases in May, 1895. The affection soon after died out, but it reappeared in the winter of 1896. I understand there have been no recurrences since the spring of 1897.

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[a] Bondurant: New York Medical, Nov. 20 and 27, 1897. Here will also be found the only published reference which I know of to the Little Rock epidemic.

An epidemic of extreme interest appeared at the asylum of Sainte-Gemmes-sur-Loire[a] (the asylum for the department of Maine et Loire) in May, 1897. The disease began very treacherously. Attention was first drawn to its existence by an unusual mortality among the epileptics who died in the status, and whose bodies were found to present considerable anasarca. Though first appearing as a severe epidemic in 1897, it would seem that isolated cases occurred in 1896 and 1895 which were recalled when the occurrence of the epidemic of 1897 threw fresh light upon the subject. It is stated that about 150 patients suffered and 40 died. The careful descriptions given of the symptomatology and morbid anatomy leave no doubt as to the identity of the affection with beri-beri in both respects. The epidemic, however, had these peculiarities—that gastro-intestinal troubles were unusually prevalent, and a peculiar form of erythematous eruption, somewhat recalling that of pellagra, was very general. I have heard of a case of beri-beri occurring in this country which presented the latter symptom, but nothing of the kind appeared at the Richmond Asylum. Three of our cases presented a transient condition of erythema nodosum, affecting the legs and lower part of thighs, appearing with the oncome of the other symptoms, and accompanied by slight fever. One case presented an eruption of large bullæ. One patient suffered from phlebitis of the cutaneous veins. In two diffuse inflammation of the highly œdematous subcutaneous areolar tissue occurred with abscess formation, and in one the appearance of traumatic cellulitis in one leg accompanied the appearance of neuritic conditions in the other as well as the cardiac signs of beri-beri. The last-mentioned patient relapsed twice afterwards without showing any tendency to diffuse inflammation. There is little, then, in our cases to point to any special cutaneous condition or tendency to inflammatory change in skin or subcutaneous tissues. Chantemesse and Raymond point out the remarkable fact that an epidemic visited the Sainte-Gemmes Asylum in the year 1854, and the following years, in which this erythematous eruption was a prominent feature, and which was accompanied by gastro-intestinal trouble. These epidemics have been described by Billod,[a] then physician and director of the asylum, under the name of "a variety of pellagra peculiar to the insane." Billod recognised that this pellagra differed from the ordinary form, and points out that pellagra presents certain local differences at its various seats of outbreak. While drawing attention repeatedly and pointedly to the difficulty of thoroughly ascertaining physical conditions in the insane, he gives a pretty full description of various "nervous" symptoms which accompanied his cases, and seemed to him to be portion of the *tout ensemble* of pellagra. These consisted chiefly of marasmus, excessive debility and wasting. In a few cases there appear to have been contracture of the limbs, and cases are mentioned in which a condition resembling general paralysis was brought about. A certain degree of œdema of the lower limbs appears to have been very common, and sometimes there was more general dropsy. Dropsical conditions are often mentioned in the accounts of autopsies. It is mentioned in one case that walking or even standing was impossible, that the wasting was intense, and that the lower extremities were œdematous. It is true that Billod did not suspect paralysis. On the other hand, in describing a condition which he found, or thought he found, in several cases—namely a general softening of the white matter of the spinal cord—he draws the attention of physiologists to the singular fact that so remarkable a change could occur in the spinal cord without entailing on the patients who presented it any paralysis either of movement or of sensation! Nevertheless there seem to be some grounds for believing that Chantemesse and Raymond may be correct in conjecturing that Billod's pellagra was really beri-beri, and identical with the affection which has recently visited Sainte-Gemmes. If this be not so it is strange that similar cutaneous troubles should have appeared in two distinct diseases occurring at such an interval in the same locality.

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[a] Une épidémie de paralysie ascendante chez les aliénés rappelant le beri-beri. Chantemesse et Raymond. Annales de l'institut Pasteur, XII., 9. Sept. 25, 1898.

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[a] Archives Générále de Médecine, 1858. Vols. I. and II.

In the German asylums of Grafenberg and Alt-Scherbitz[a] sporadic cases of peripheral neuritis have occurred which seem to resemble beri-beri.[b]

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[a] Zeitschrift f. Psychiatrie. B. LV. H. 1.

[b] LITERATURE OF BERI-BERI.—The best book on beri-beri is Scheube's "Die Beri-beri Krankheit," Jena, 1894—a model of accurate observation and extensive erudition. Pekelharing and Winkler's "Recherches sur la nature et la cause du Béri-béri et sur les moyens de la combattre," Utrecht, 1888, contains much valuable information. It is now accessible to the English reader in the translation by Mr. James Cantlie. Subsequent observers have not altogether borne out P. and W.'s views as to the bacteriology of the disease, which, I understand, have been relinquished even in Holland; but the clinical part of the book is excellent, and a comparison with Scheube shows the identity of the kakké of Japan with the disease observed by the Dutch in Sumatra and Java. The best English account of the disease is the full, accurate, and elegantly-written article by Dr. Patrick Manson in Davidson's "Diseases of Warm Climates." Shorter but of great excellence is Dr. Manson's notice of beri-beri in his "Handbook of Tropical Diseases." Professor Anderson's "Lectures on Kak'ké," Yokohama, 1879, are also very valuable; see also the same author in "St. Thomas' Hospital Reports," 1876. Some of the very early English writers—Mason Good, Ridley, and others—gave good descriptions of beri-beri. Then for some time our countrymen writing on this subject, generally army surgeons, were mostly led astray by the pursuit of theoretic views as to ætiology and by endeavours to uphold certain opinions which might be termed official—viz., that what was called beri-beri was merely anæmia, or anchylostomiasis, or the like—and so with few exceptions produced work of little value. Grimm's "Klinische Beobachtungen

über Beri-beri," Berlin, 1897, is a valuable and original monograph. An immense number of papers in medical journals by various Dutch, Portuguese, German, and French authors have appeared. The Dutch and Portugese I know only at secondhand. Among the most valuable of the German are those of Bälz, Miura, Weintraub, Wernich, Jelgersma, &c. Among the French may be mentioned Déchambre, Durand, Féris, Le Roy de Mérincourt, de Lacerda, Marie, &c. A very full bibliography is given at the end of Scheube's monograph, and this has been brought up to date in the article on beri-beri in his more recently-published "Diseases of Warm Countries" (1896). The total of works referred to by Scheube is close upon 400.

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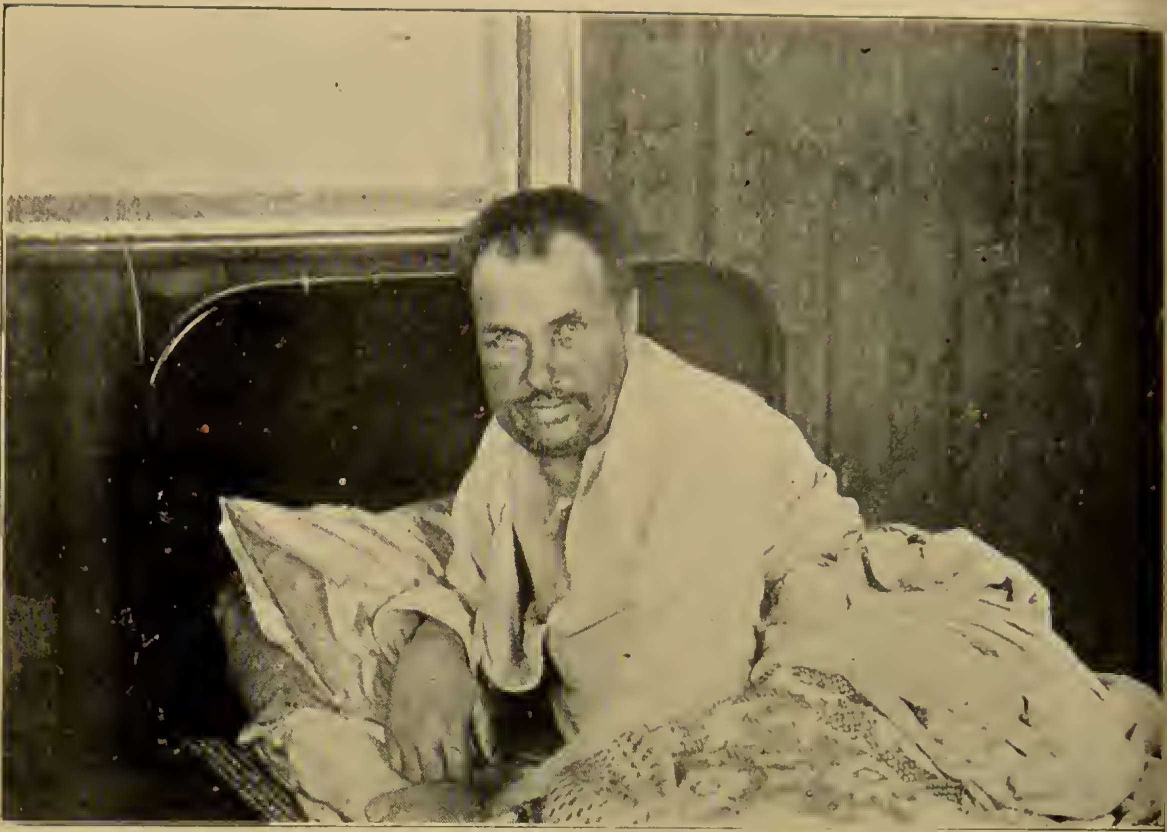

Plate I.

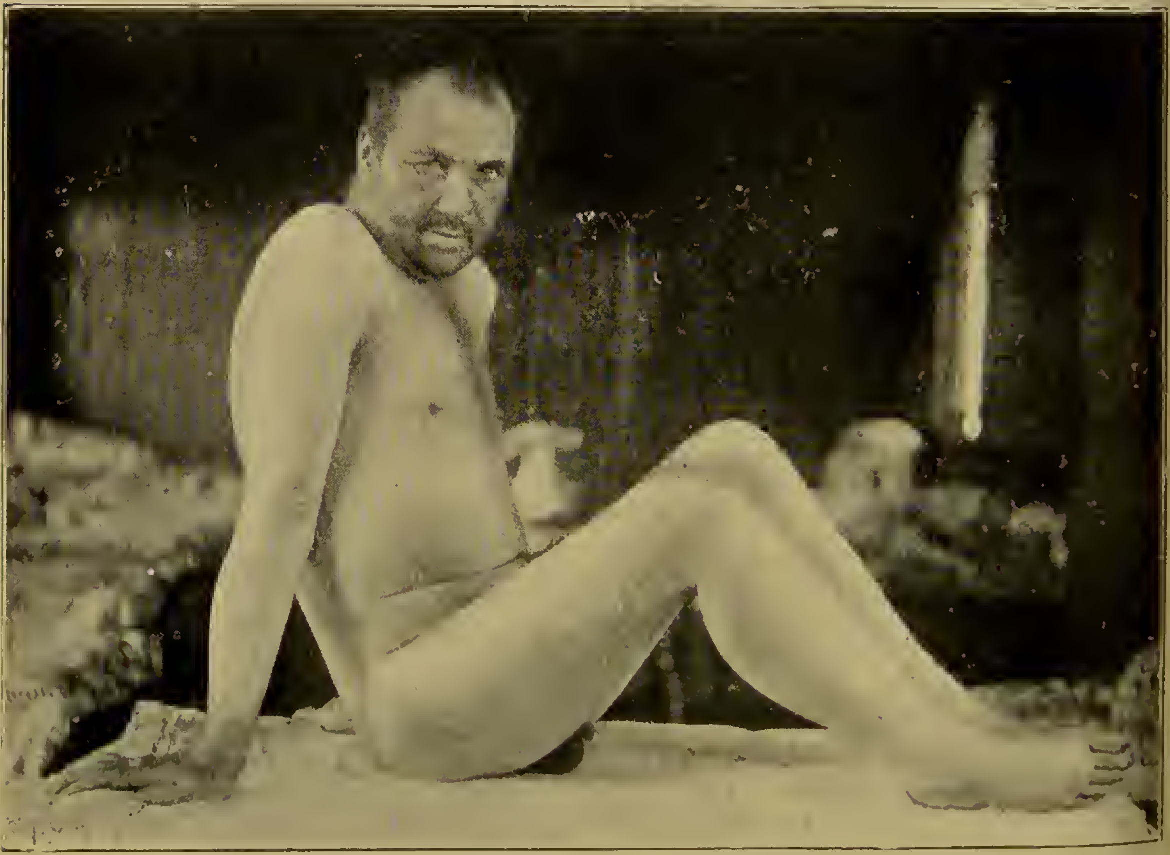

Plate II.

T. G.—*General Anasarca.*—Patient was unable to walk and progressed on his hands an buttocks, in the attitude shown in Plate II.

[*From photographs.*]

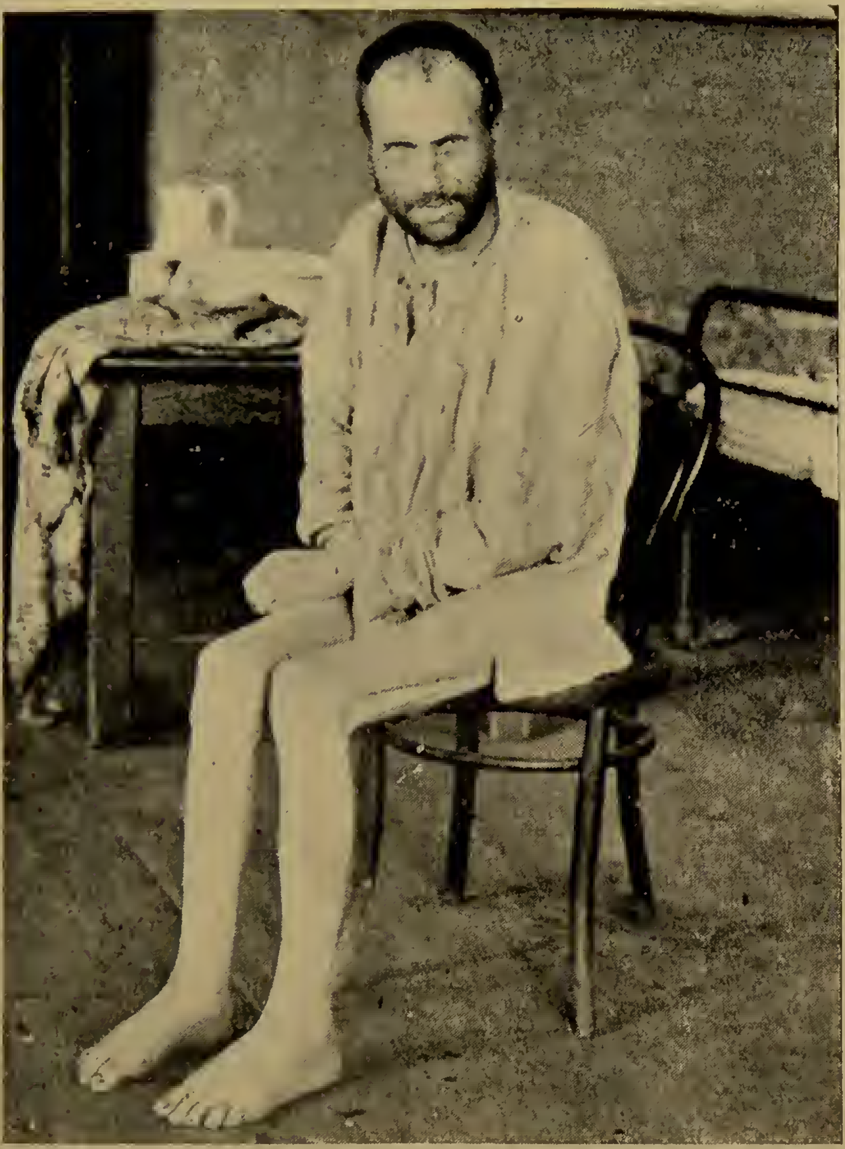

PLATE III.

T. G.—*Atrophic stage*, subsequent to general anasarca. This patient (shown also in Plates I. and II.) suffered in the epidemic of 1894, and made a good recovery.

[*From a photograph.*]

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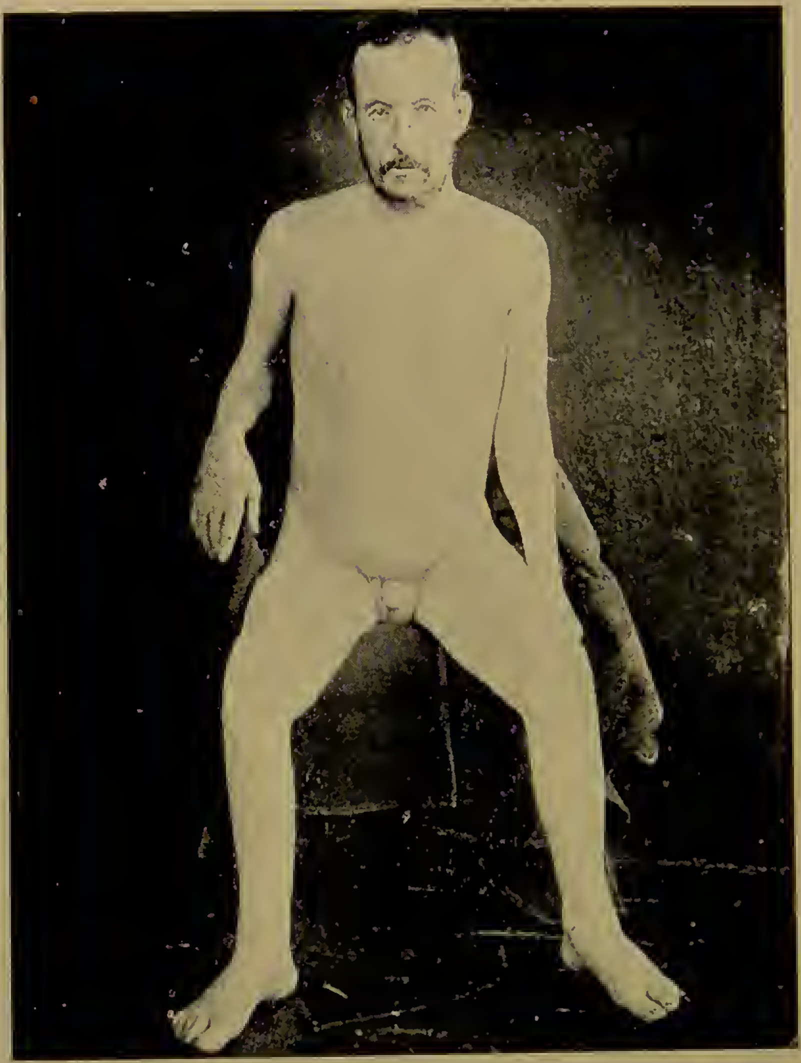

Plate IV.

H. McK.—General œdema.

(Epidemic of 1896.) [*From a photograph.*]

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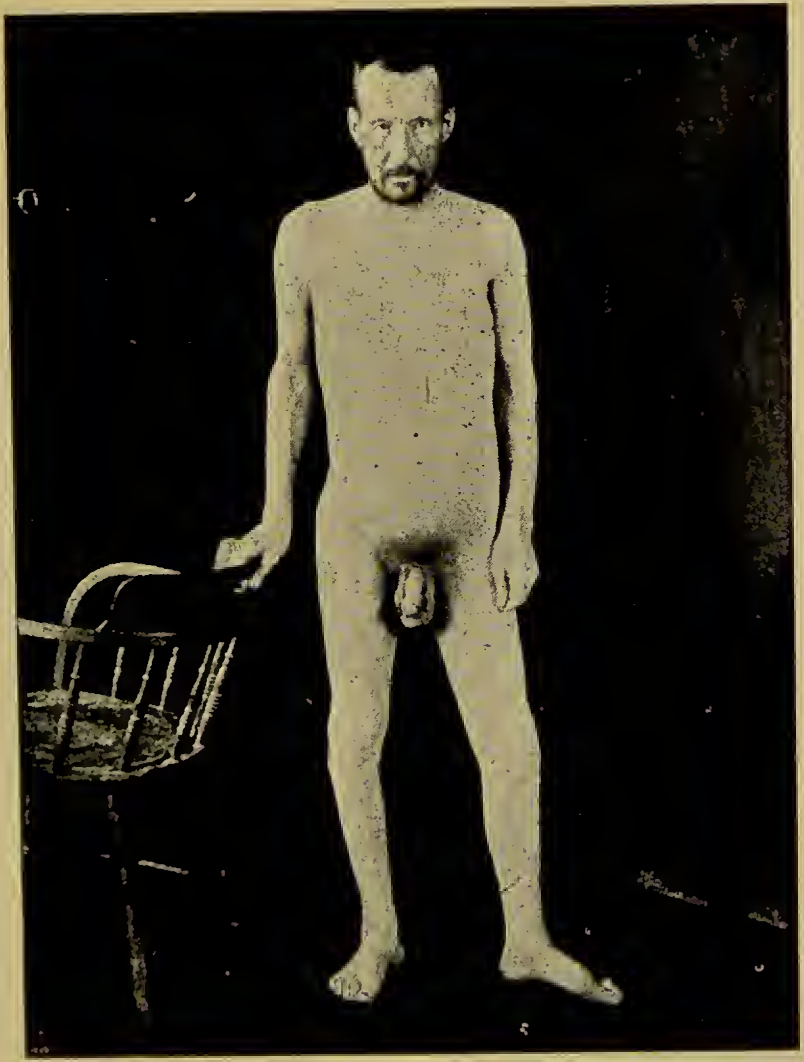
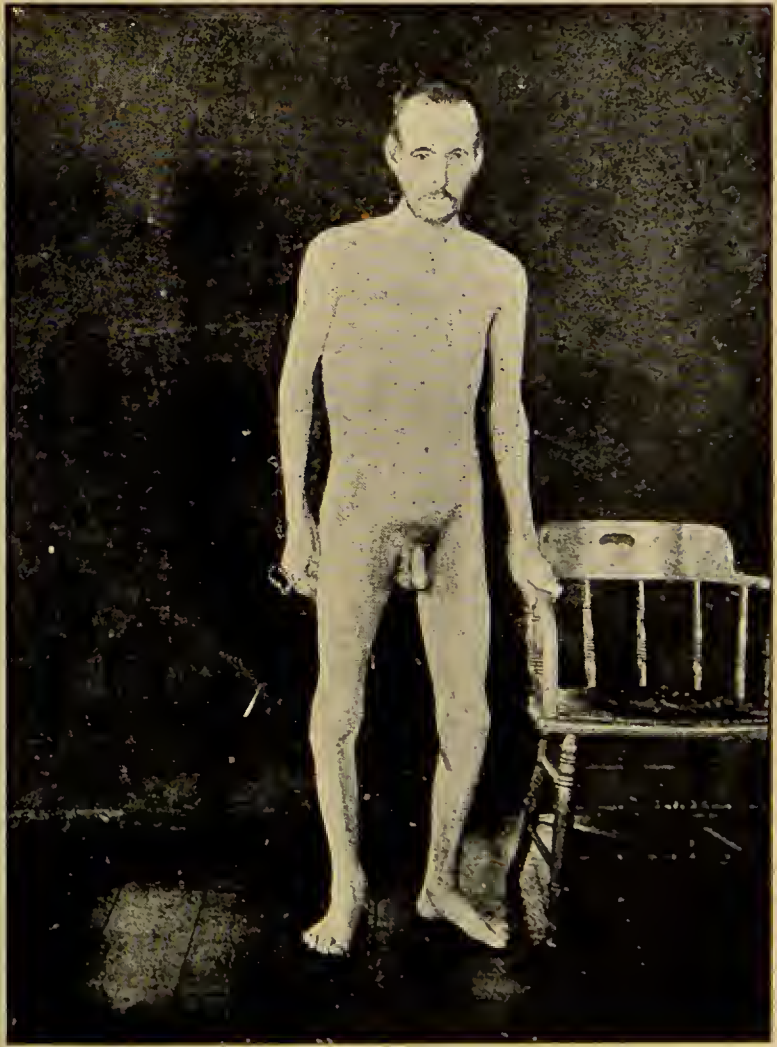


V.
H. McK. Œdema subsiding.



VI.
H. McK.—Œdema subsided; wasting manifest.

[*From photographs.*]

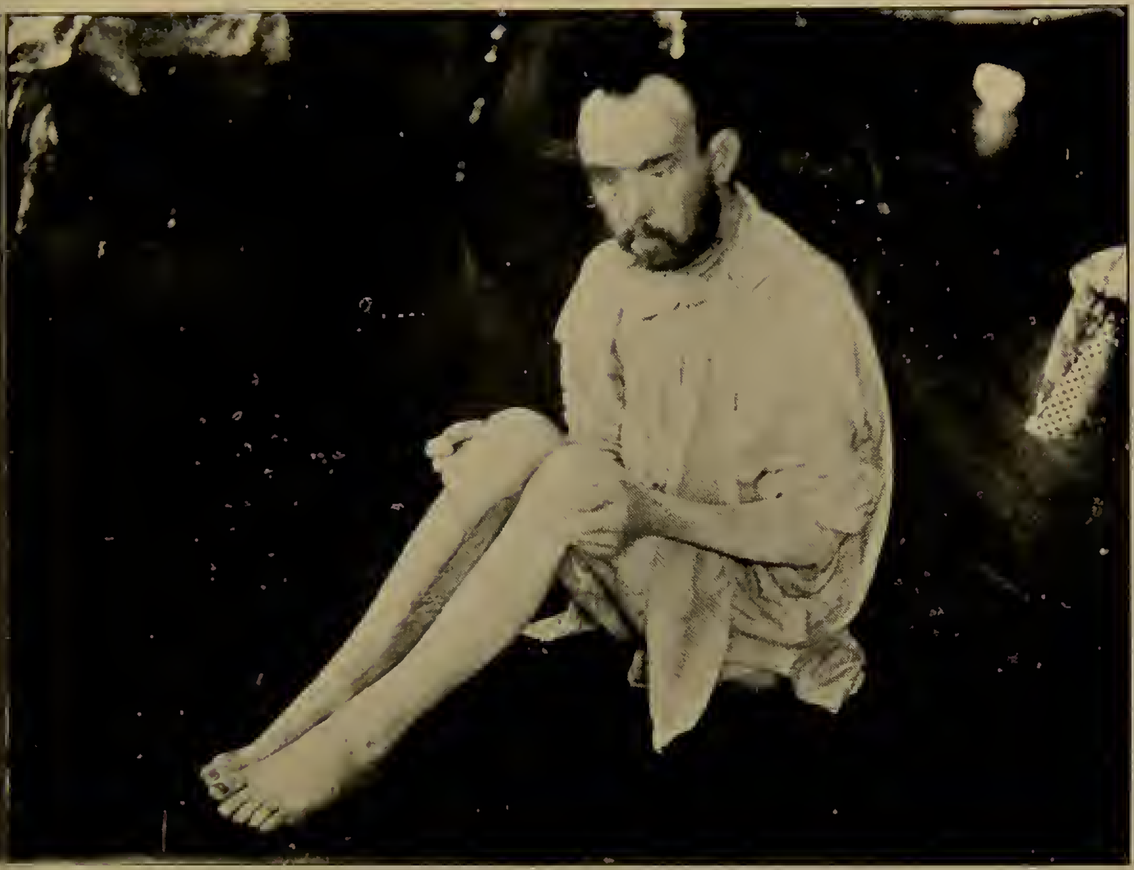


Plate VII.

M. B.—Patient, unable to walk, moved himself along the ground on his buttocks. Pointing of feet, and flaccidity of wasted calf muscles.

(Epidemic of 1894.) [*From a photograph.*]

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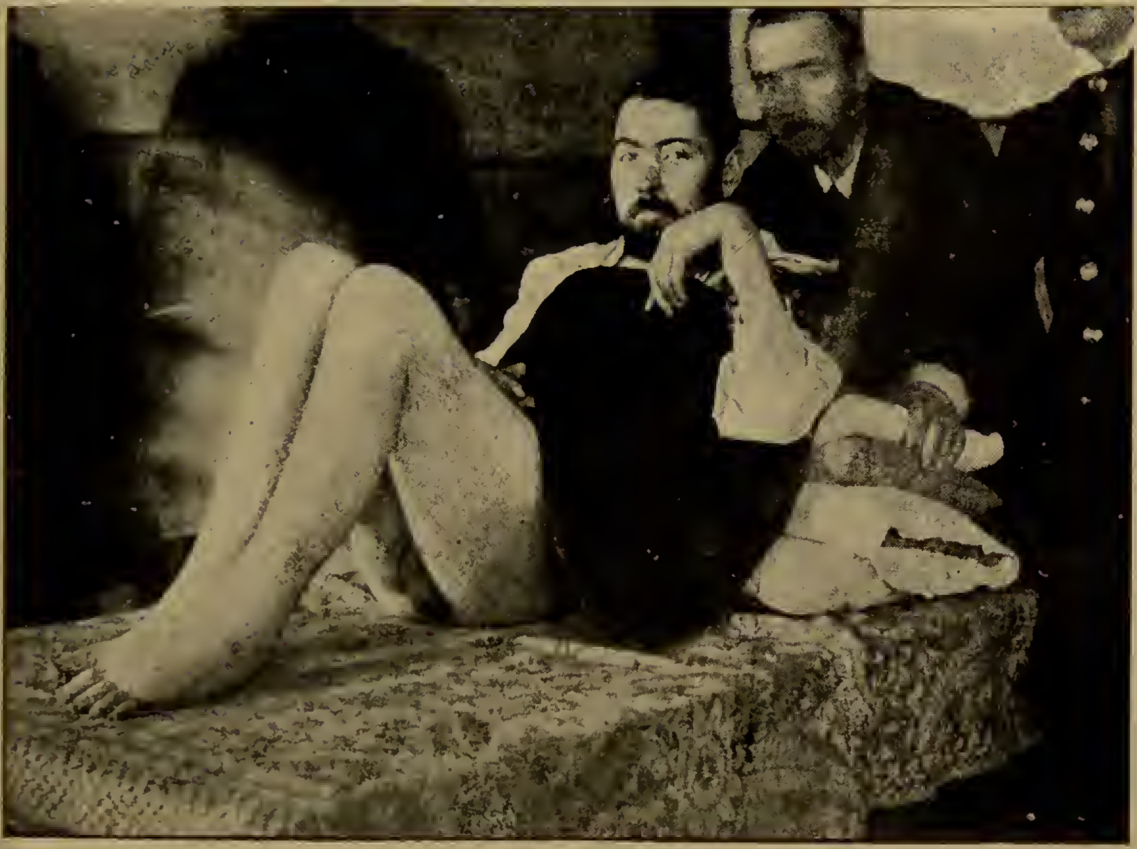

Plate VIII.

O'R.—Well-marked drop-wrist; face slightly puffy; well-marked œdema of leg; drop-foot.

(Epidemic of 1894.) [*From a photograph.*]

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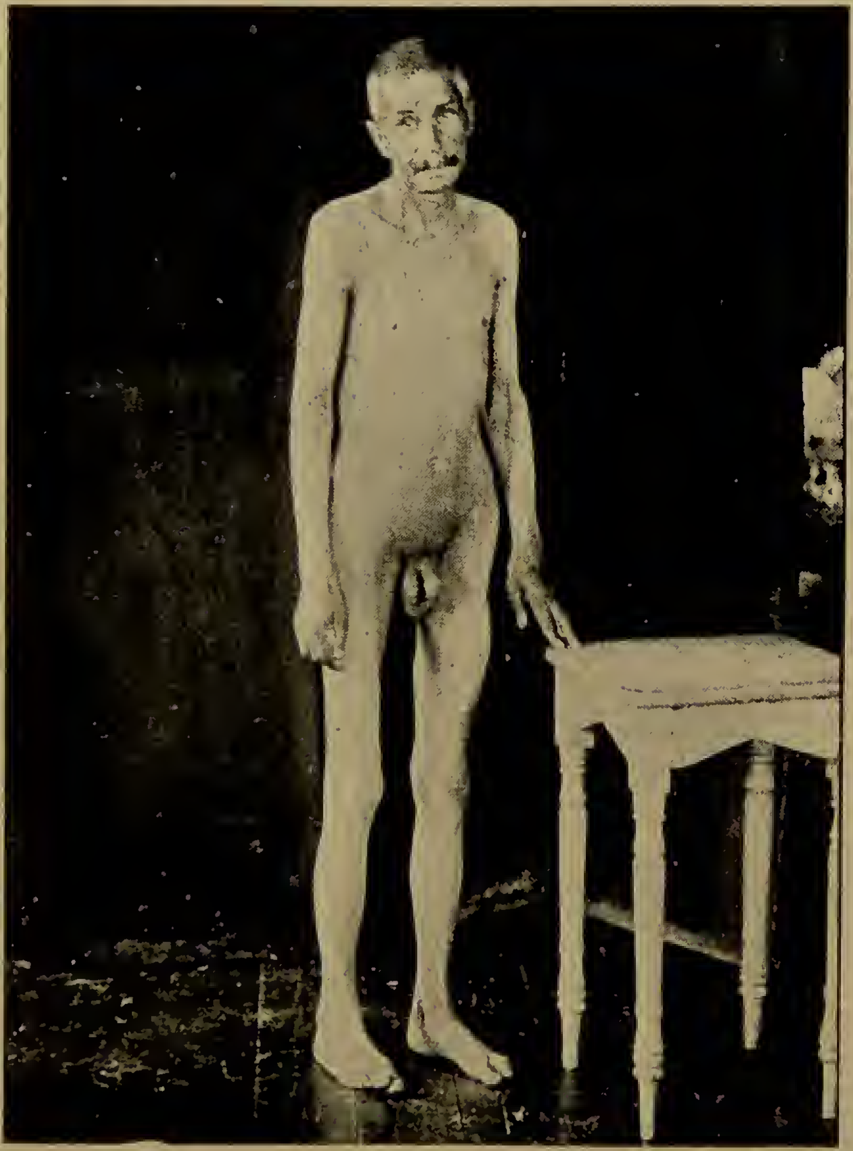

Plate IX.

J. M.—Marked wasting of muscles in "Dry" beri-beri.

(Epidemic of 1896.) [*From a photograph.*]

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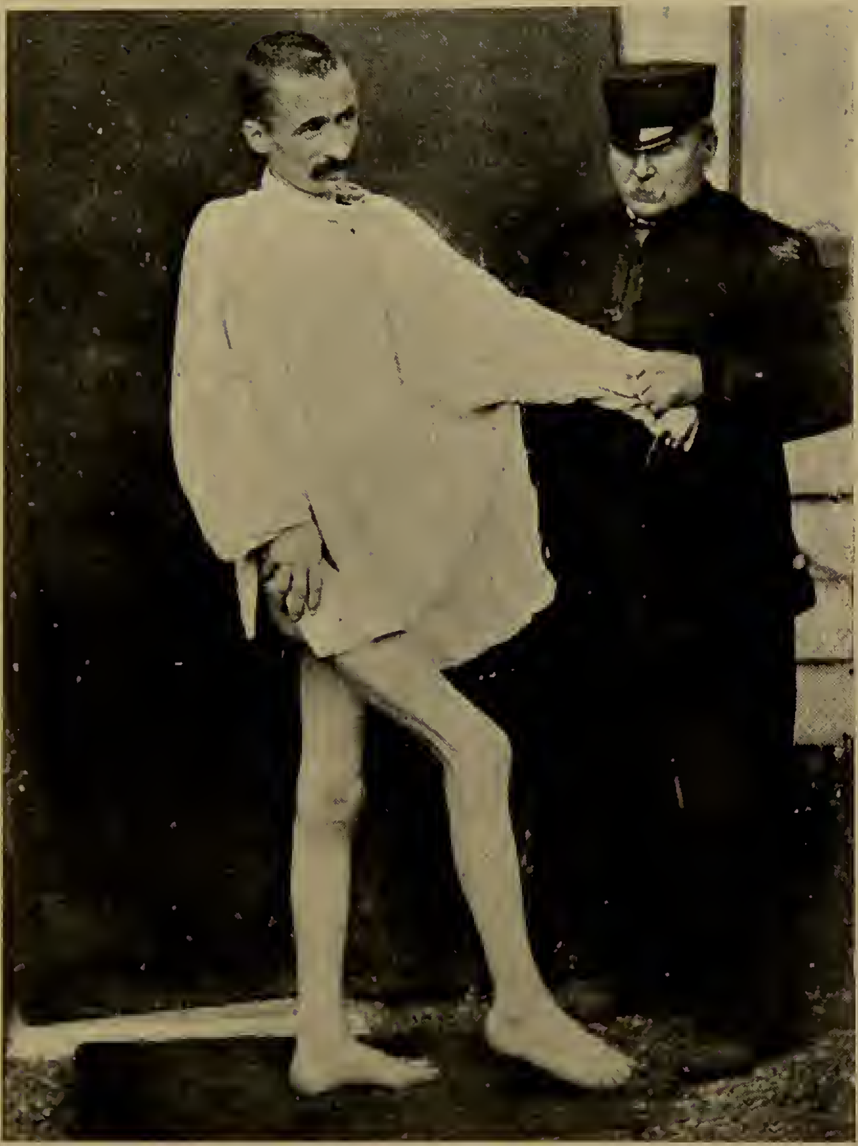

PLATE X.

H. S. R.—An attempt to show the "démarche du stepper." In this case there was marked but transitory œdema, followed by wasting which existed when this photograph was taken.

(Epidemic of 1896.)

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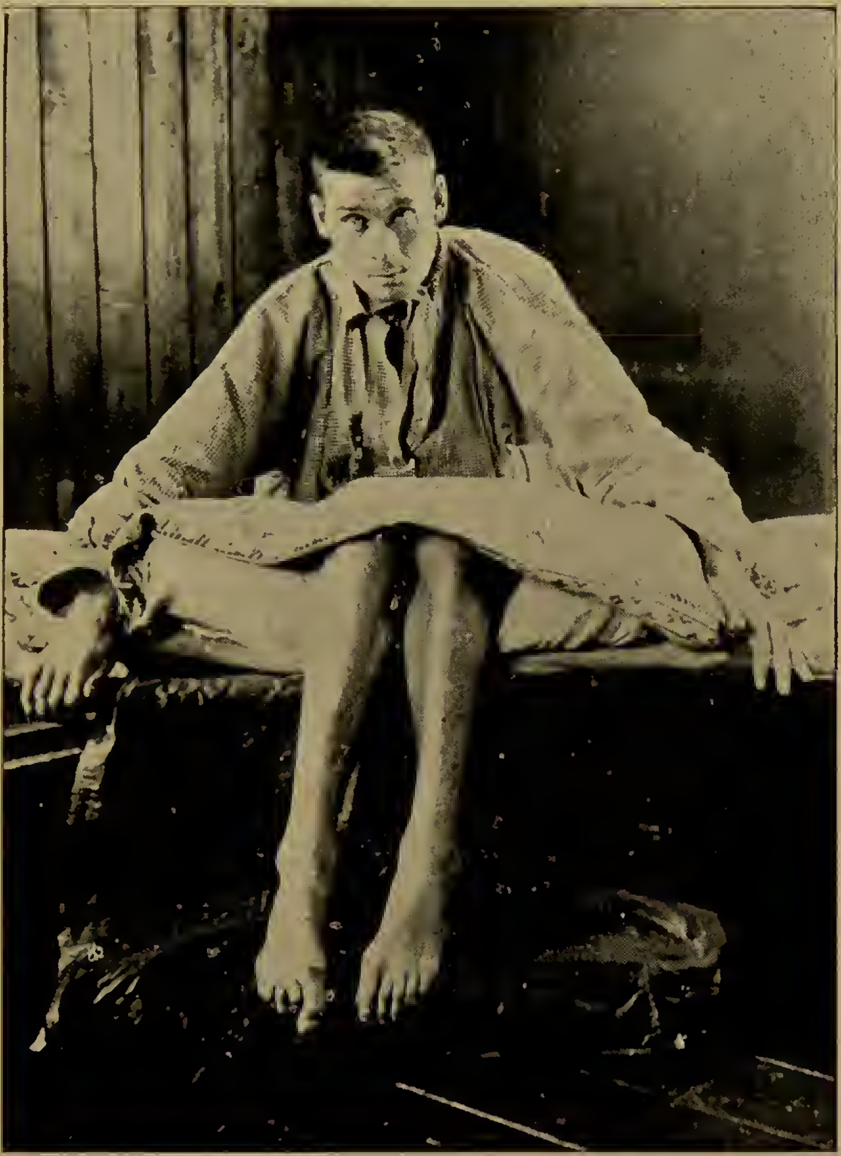

PLATE XI.

J. K.—Dropped, wasted, and inverted feet and legs. The feet subsequently became contracted and fixed in this posture.

(Epidemic of 1894.) [*From a photograph.*]

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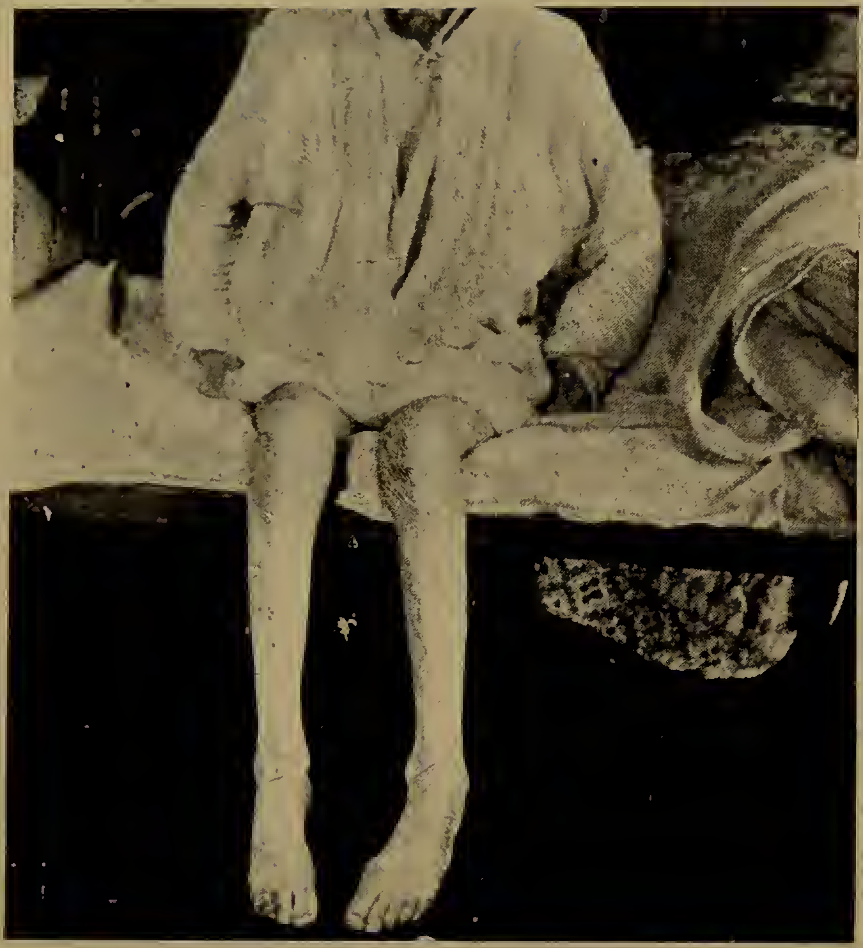

Plate XII.

B. U.—Showing atrophy of leg muscles. There had been initial œdema, which recurred from time to time. Showing also dropped inverted feet.

(Epidemic of 1894.) [*From a photograph.*]

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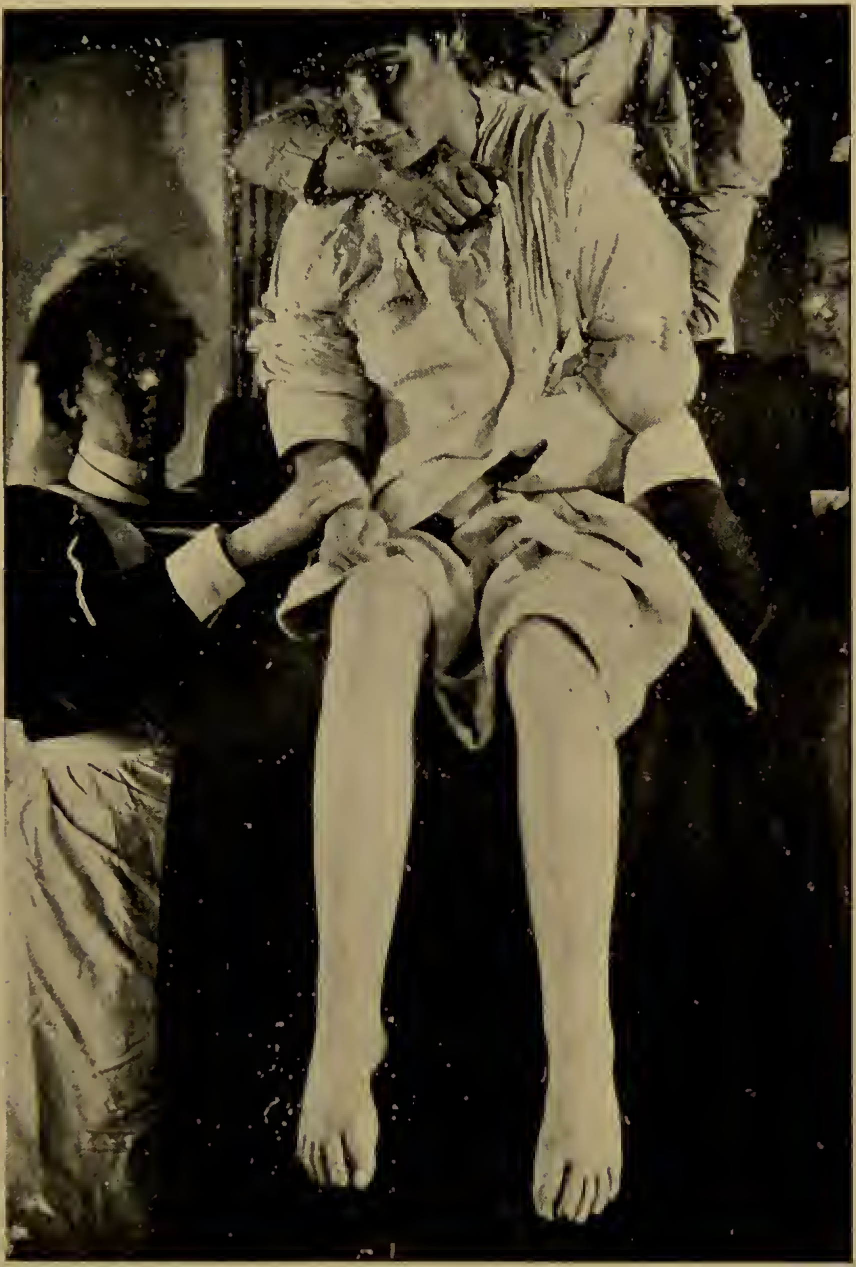

PLATE XIII.

M. F.—Dropped, inverted feet; second toe riding; muscles wasted, yet some solid œdema of superficial tissues. Patient, who was a low type idiot incapable of speech, after exhibiting characteristic steppage, had become, when this photograph was taken, incapable of walking or standing.

(Epidemic of 1897.)

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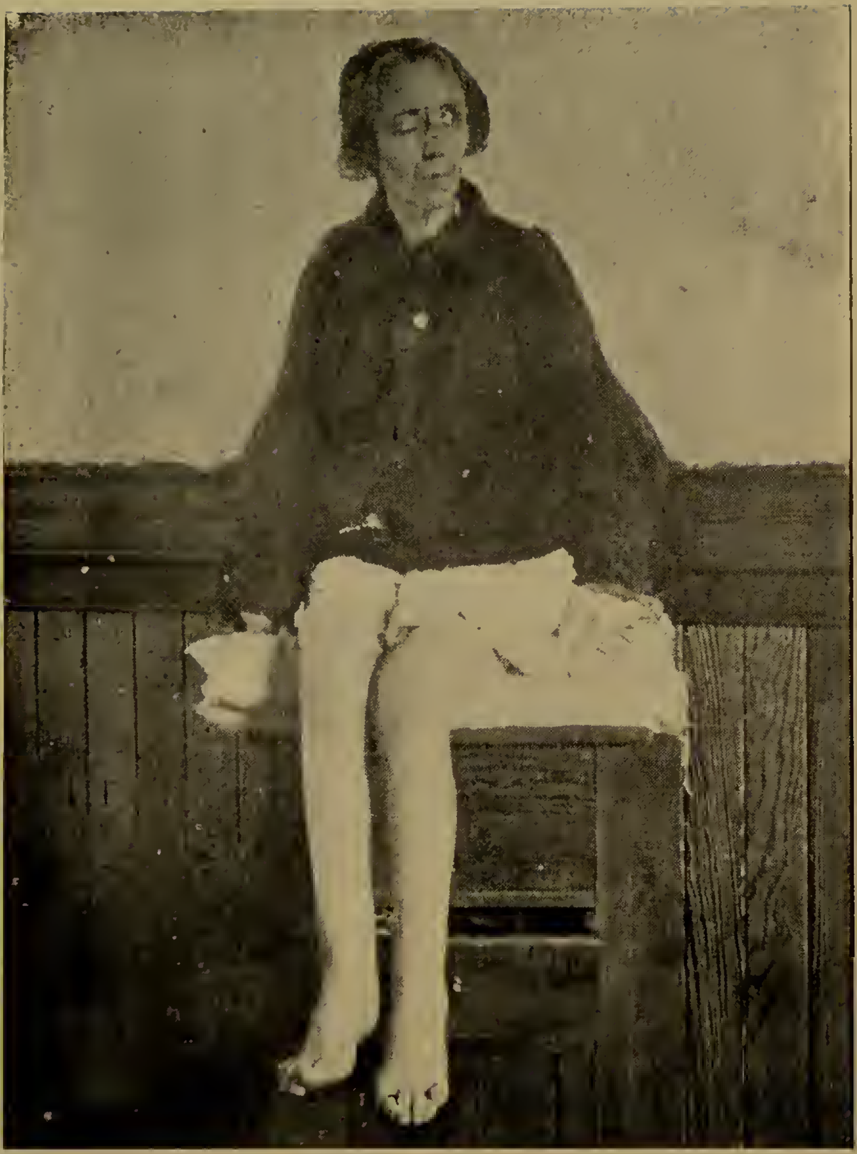

Plate XIV.

B. B.—Third-nerve palsy ; solid œdema of legs.

(Epidemic of 1897). *[From a photograph.]*

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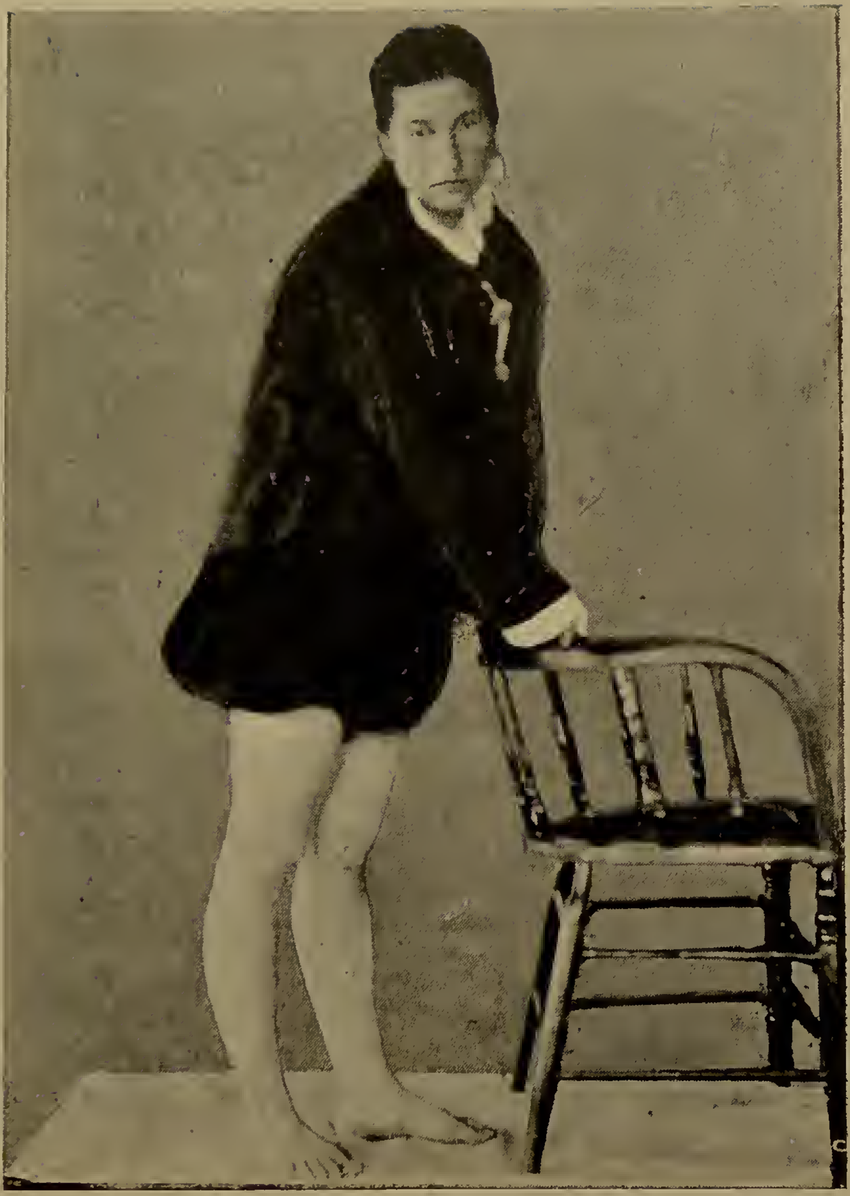

Plate XV.

M. B.—When this photograph was taken œdema was not marked. Patient could not walk nor stand without support. When she stood the knees tended to bend backwards.

(Epidemic of 1896.)

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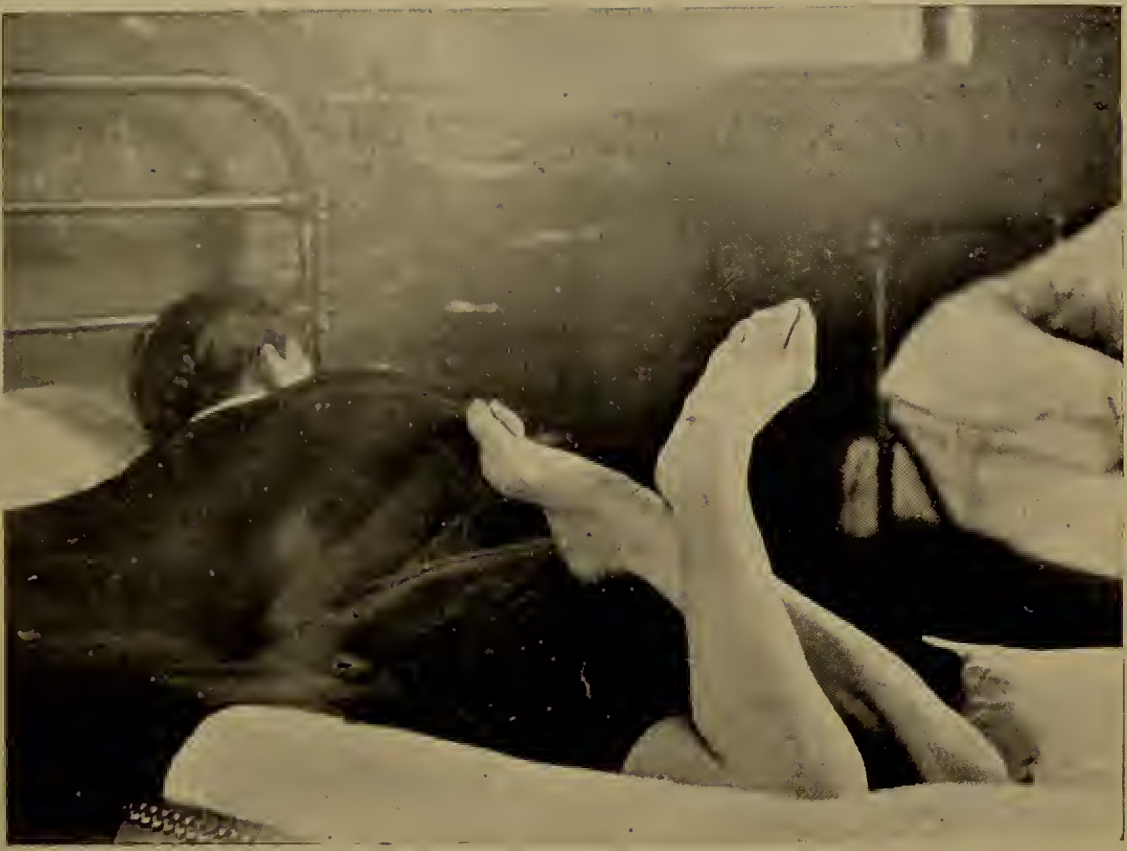

PLATE XVI.

M.D.—To show the relaxed condition of knees and ankles. The patient is as flat as possible, yet the heel having been let fall upon the buttock remains in that position; the foot also falls about under the influence of gravitation. (Epidemic of 1897).

[*From a photograph.*]

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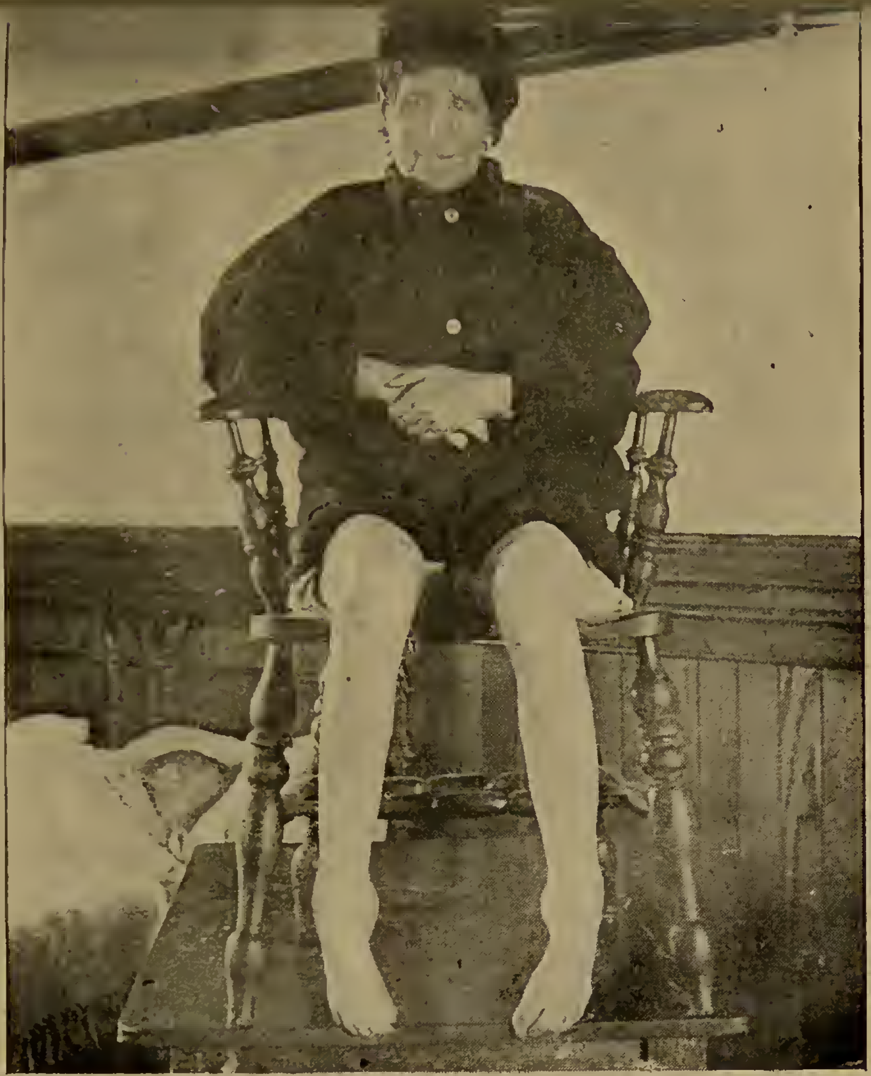

Plate XVII.

M. B.—Showing drop-foot; riding 2nd toe; contracture of great toe; inversion of foot; wasting of leg.

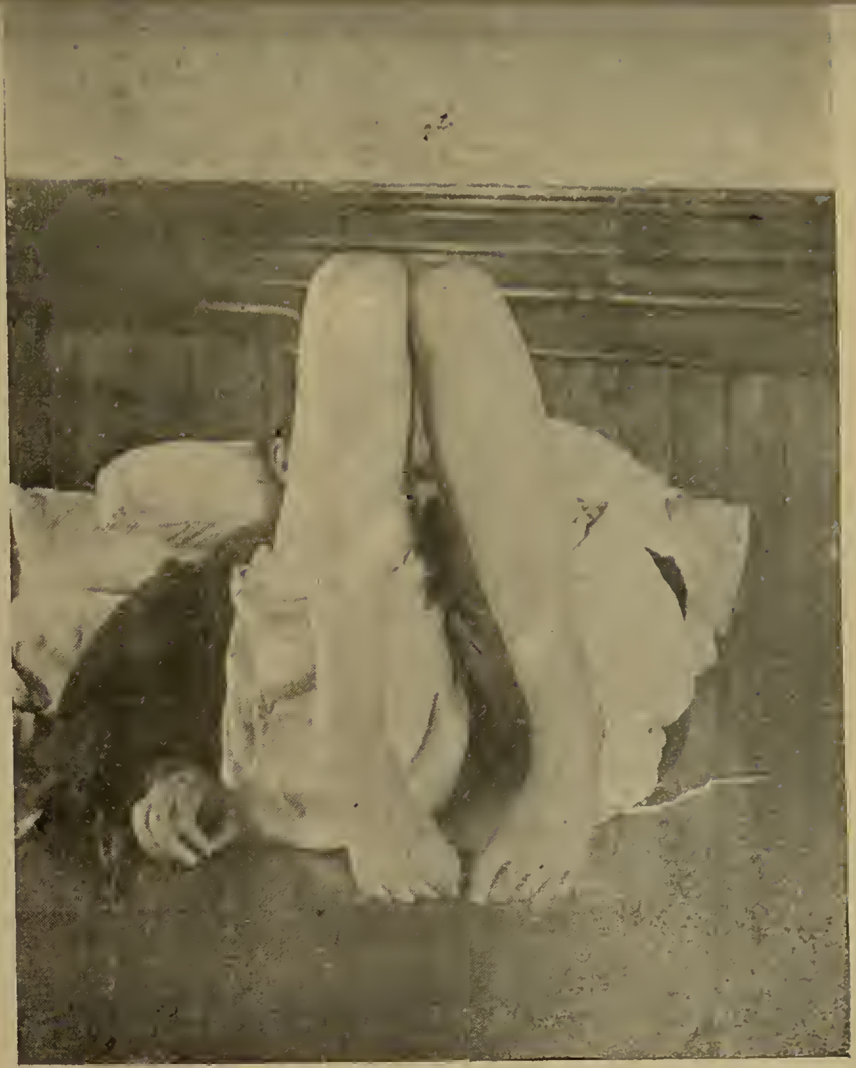

Plate XVIII.

M. B.—Showing inversion of feet; tendency of 2nd toe to ride: contractures of great toe; extreme relaxation of knee-joints allowing with ease the heel to buttock posture; also wasting of calf muscles.

(Same patient: epidemic of 1895.)

[*From photographs.*]

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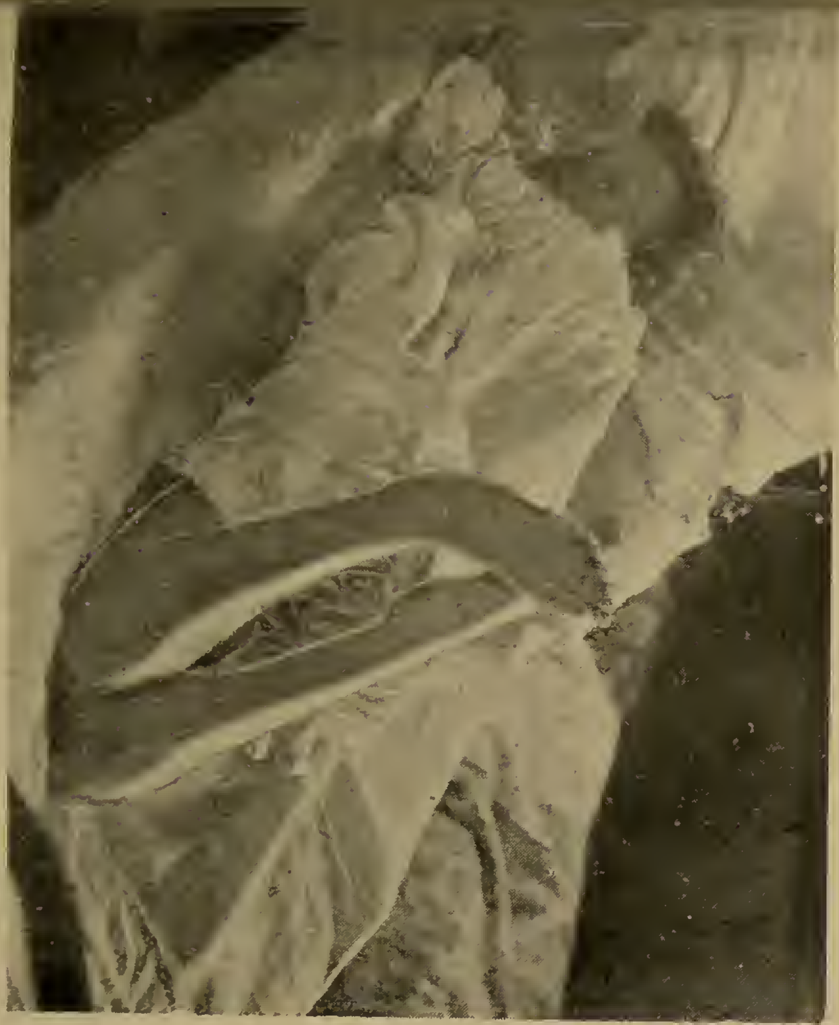

Plate XIX.

L. McP.—Shows extreme relaxation of knee and ankle joints. The heels rest upon the buttocks, and the feet fall forwards under the influence of gravitation.

(Epidemic of 1896.) [*From a photograph.*]

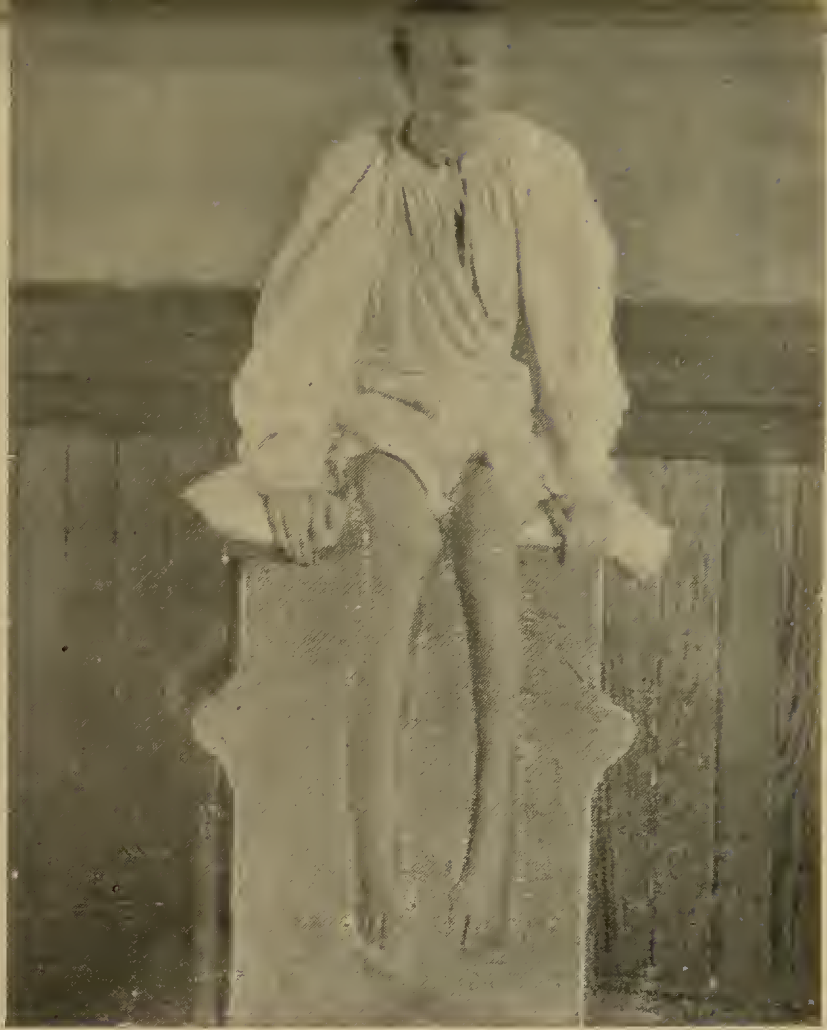

Plate XX.

L. McP.—This photograph shows extreme atrophy of leg muscles with dropped inverted feet. Œdema was not observed as preceding atrophy when patient was first attacked in 1896. Subsequent attacks in 1897 and 1898 were ushered in by a considerable degree of solid œdema.

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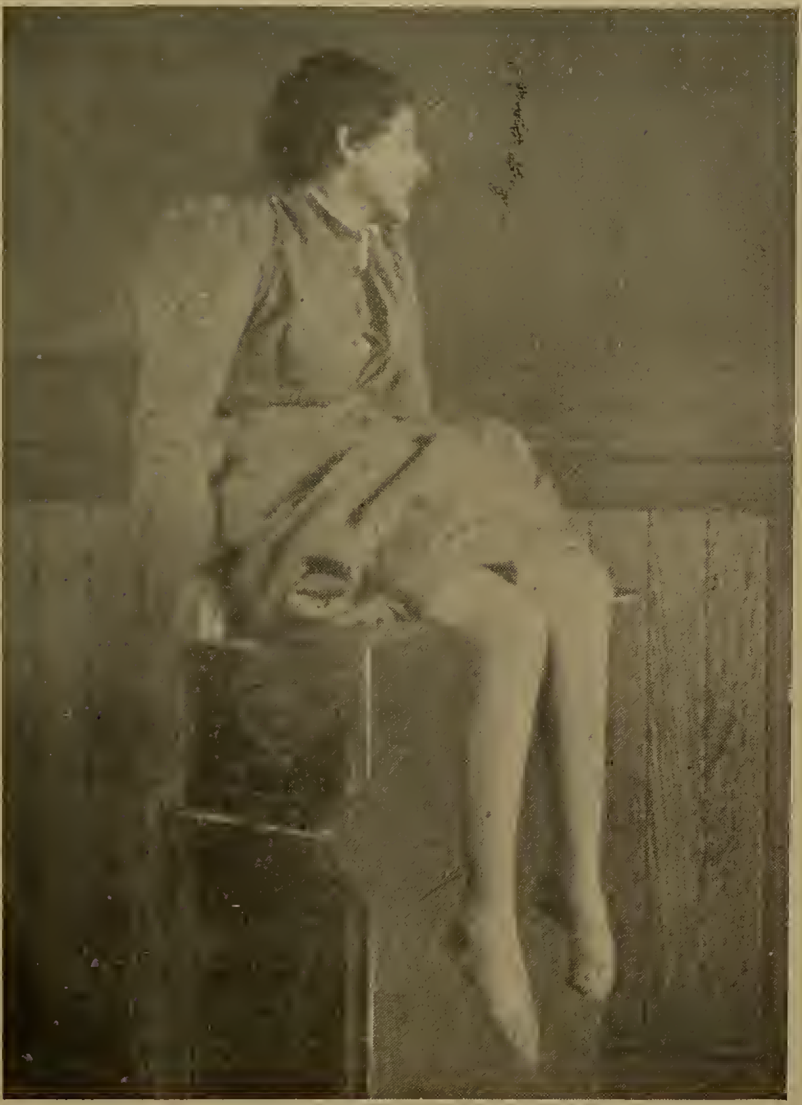

Plate XXI.

L. W.—Atrophied leg muscles. Dropped inverted feet. Contracted left great toe. When this photograph was taken patient was unable to walk. She subsequently regained considerable power. Several relapses, accompanied by great œdema of the legs.

(Epidemic of 1896.)

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Reprinted from *The Indian Medical Gazette*, Vol. XXXV
(No. 12, Dec. 1900).

THE CAUSE OF BERI-BERI.

BY

E. R. ROST,
CAPTAIN, I.M.S.,
Civil Surgeon, Meiktila, Burma.

Reprinted from *The Indian Medical Gazette*, Vol. XXXV
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THE CAUSE OF BERI-BERI.

BY E. R. ROST,
CAPTAIN, I.M.S.,
Civil Surgeon, Meiktila, Burma.

My attention was first called to this disease in an outbreak of beri-beri at Meiktila Jail in 1898; at that time I thought the disease was due to a micrococcus, which I found in between the starch cells in *jewary*, in the granary of the jail; I had also found it in pigeon's excreta from the roofs, and thought I had also found it in the blood and in pigeon's blood. But my series of experiments were open to considerable objection as regards method, as I have now learned. It was about the same time that a paragraph appeared in the *British Medical Journal* of the 24th September, 1898, concerning the connection between rice and beri-beri. It was not till coming to Rangoon in May 1900 that I had the opportunity of seeing more cases of beri-beri and of carrying out a series of experiments, which are now about to be described.

Working on the idea that beri-beri is a rice disease, of the various ways in which rice is brought into connection with the body, the one which appeared most likely to bring forward light on the subject was the rice liquors which are so largely consumed by the coolie classes of Rangoon.

Several bottles of different kinds of rice liquor, the conjee, the brown rice-water liquor, and the white rice-water liquor sold for next to nothing in the bazaars were given me for examination, and the organisms found therein were identical and were found to emanate from between the starch cells. Moreover, the same organism was found in damp rice, was also found in a pellet of yeast which the Chinese use to ferment rice-water with, and which they obtain from Singapore (refusing to tell what it is).

At the same time after prolonged examination of blood of beri-beri patients, which was obtained by a method to be described, the same peculiarly shaped organisms were noticed, and they were later found in the cerebro-spinal fluid and in the serous exudation in the sheath of the sciatic nerve *post-mortem.*

Cultures in sterile rice broth, in beef broth, in blood, in hydrothorax fluid, in ascitic fluid were made, and it was in these cultures that the morphology of the organism was observed.

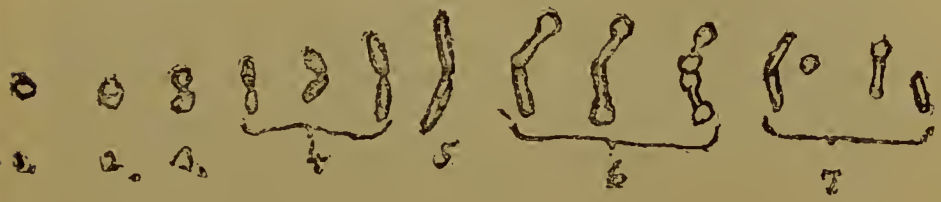
In carrying out controls of rice broth it was found that it was with extreme difficulty that the organism could be killed, and a temperature of 220°F. for nine hours was found to be necessary to kill off the spores

Firstly, four cocks were injected intra-peritoneally from the cultures obtained from rice-water, and they all had reactions, though they recovered.

Then cultures from the cerebro-spinal fluid and from the blood in broth, in blood serum and in rice broth were injected into fowls, and the disease has been communicated to the fowls, the organism being found in the blood and in the spinal cord, the animals dying with the same peculiar symptoms.

A goat and guinea-pigs were also injected, and they are still under observation, as are other fowls.

The organism is a diplo-bacillus, which generally is seen as an angular organism; it develops by spores, the spores split into two, become elliptical and grow out into rods, so that the following different shapes may be seen from time to time.



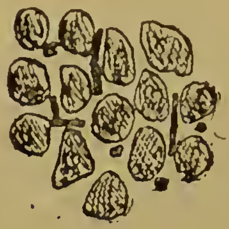
Between the starch cells in rice may be seen micrococci (really spores) and occasionally the angular diplo-bacilli lying between the cells.

The organism is very active and moves along, wagging one rod in front of the other.

Double dumb-bells are seen, single knobs or rods, which have broken off in consequence of the heavy knobbed end of its partner.

Sometimes one of the rods points up, so that one thinks one sees a knobbed single rod, whereas in reality it is only an angle sticking vertically up in the line of vision.

The organism is stained easily by carbofuchsine. After growing on different media to some generations it alters in size considerably. It multiplies with great rapidity, will grow best in rice broth, ascitic fluid, hydrothorax fluid, broth,



I.

Organisms seen between the starch cells in rice.

blood serum, with difficulty or not at all on solid media, except coagulated blood serum.

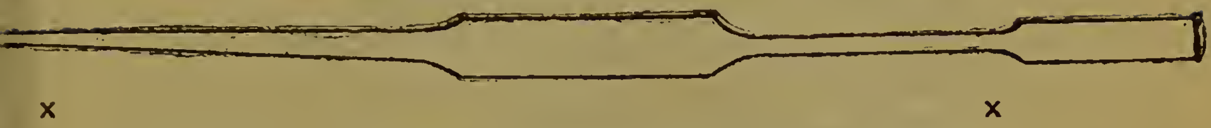
To test its vitality a number of tubes of cultures in rice broth were put in the steam sterilizer and taken out every hour or half hour and placed back in the incubator. It was found that after eight hours at 220° F. with a slight increase of atmospheric pressure the cultures were still obtainable, but after nine hours the tubes gave negative results. After finding this out experiments were carried out afresh, and all the media used in cultures were sterilized for long periods.

The method I use in obtaining blood is by making glass pipettes with a long capillary pipette, a chamber, a second capillary pipette, and then a tube to fit a syringe on to, for suction.

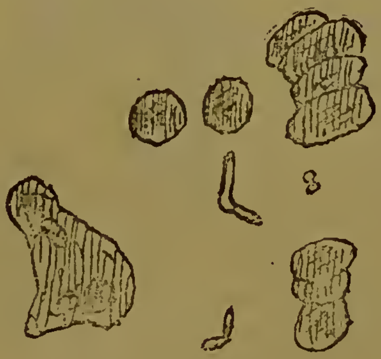
The end is sealed in the flame, and the making of the pipette ensures its sterilization.

When required to be used, the end is broken off with forceps, a vein is made prominent and the skin prepared, the glass capillary is run directly into the vein, if it gets well in the blood will flow, and for obtaining a perfect specimen it is well to allow the blood to flow a little through the tube, the pippette is then sealed at X. X.,′ and the blood may be examined when convenient.

When examined, one end of the pipette is broken off, and the other is held near the flame; this sends out one drop from the open end, which is caught under a cover-slip held in iridectomy forceps. The cover-slip has been removed from alcohol and dried in hot air, not touched with anything but the points of the iridectomy forceps.



The cover-glass is placed gently down and the specimen examined. I find 6th inch with No. 4 eye-piece all that is required, and after a very careful examination the organism in one of its morphological states will be seen; the most certain is the angular condition.



V.

From fresh specimens of beri-beri blood.

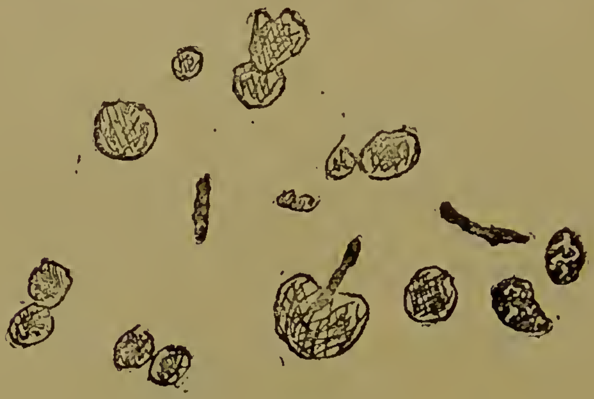
I have examined 32 cases of beri-beri by this method, on numerous occasions (three of these were *post mortem*). I have found the organism in every one of the cases on each occasion.

The veins of the foot were used at first, but now it has been found with equal success in the veins of the arm.

A very careful examination of one specimen perhaps of one field for a long time will alone enable you to see the organism. I have watched small round bodies like those which are normally found in the blood and seen them to suddenly come up (the rod had been vertical).

Blood thus obtained and incubated for 24 hours at 37°c. is found afterwards to be full of the same angular organisms.

Blood thus obtained kept under a cover-glass surrounded by vaseline has been watched, and the organisms have been watched increasing.



IV.

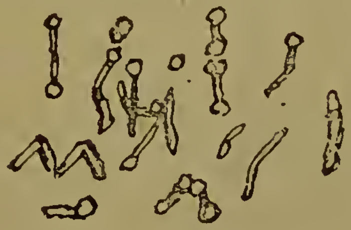
From stained specimen of beri-beri incubated blood.

The cerebro-spinal fluid was obtained by the same method, a hole being drilled into the skull; the pipette was run straight into the lateral ventricles of the brain ; in one case the cerebro-spinal fluid rushed out; in the other two it had to be drawn out by suction.

The heart blood has been always found to contain the organism.

The cerebro-spinal fluid obtained from the mid-dorsal region from a case of beri-beri was inoculated into:—

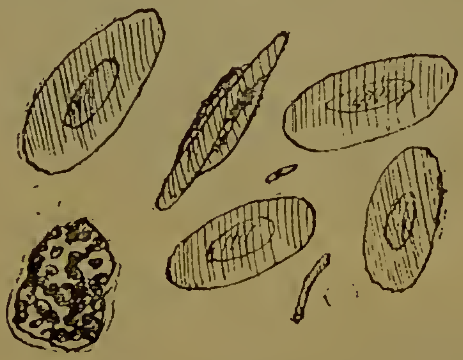
1. Broth.
2. Rice broth.



III.
Organisms sporulating, from broth culture.

After 24 hours at 37° C. 1 and 2 were full of the angular diplo-bacilli.

One cc. of 1 was injected into the peritoneal cavity of No. 1 fowl by the pipette method and 1 cc. of 2, into No. 2 fowl. On the second day fowl No. 1 fell from 106·4 (normal) to 101·4; it was extremely ill and died on the third day.



I.
From injected Fowl.

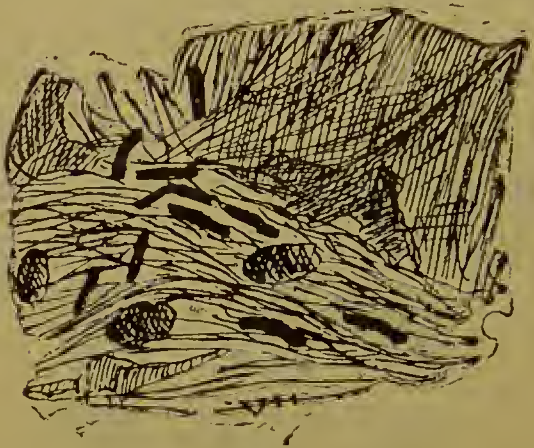
Post-mortem nothing was found, but angular organisms in its blood and spinal cord.

No. 2 fowl died on the twenty-seventh day, gradually. It had been noticed to get thinner and thinner, although it fed well and its companion control fowl was well nourished.

It was then noticed that it could not run; on being forced to run it fell over or missed its footing; it also had a peculiar uncertain walk. Towards the end its temperature fell, it became very blue, refused to eat, fly or walk and stood up on a stool in a curious attitude; it finally could not get up when turned over and died slowly.

The organism was found in its blood at stages during its illness, and the eosinophilous white blood cells were very much increased, the white cells were about 1 to 3 red.

Post-mortem.—The heart was enlarged; the kidney contained a cheesy matter which was found with the angular organisms.



VII.

Spinal Cord of Fowl.

The weight of the fowl before injection was 18 ozs., before death 10 ozs. 2 drms.

Fowl A was inoculated with cerebro-spinal fluid, and fowl B with heart blood from a case of beri-beri.

Fowl B died on the twenty-second day, fowl A on the 23rd day.

The symptoms were identical with those in fowl No. 2.

Fowl B weighed 16 ozs. on admission and 10 ozs. before death.

Fowl A fell from 18 ozs. to 9 ozs.

The peculiarity in the wasting was that all tissues wasted equally, fat being present at time of death.

The control fowls were well.

Four cocks were injected from cultures made from rice liquor, and the temperature rose from 107° (normal) to 109—111° F. from the fifth to the thirteenth day; in one case there was a slight reaction and no rise of temperature. All the cocks appeared to be ill and had a defect in walking or running. They all recovered.

I visited a liquor shop in the town and examined the place thoroughly, the method of making the rice liquor is as follows:—The rice (probably full of these organisms as was the case in this instance) is steamed, and the rice is strained off, the water being allowed to ferment for three or four days, a pellet of the yeast they obtain from Singapore is added and half and half fresh rice-water, it is filled in bottles and sold.

The longer it is kept the better it is liked. The pots are never cleaned out.

I examined the old pots in this shop, and took pipette samples and found them full of these angular organisms.

Only the poor coolies drink these rice liquors, and they are in the habit of taking the stale conjee (sour) on an empty stomach. Here I may mention that it is the Madrassee coolie who chiefly suffers from beri-beri; women do not get it so much and children rarely; the reason is easily understood. Sepoys get beri-beri, and they are fond of this liquor in the early morning.

In the rice this disease appears as a fibrous clammy coating sticking the granules together.

If in a damp chamber some of this diseased rice and boiled distilled water is added, the angular organisms can be seen coming out into the fluid after some hours.

I have not yet ascertained or been able to ascertain if weevils have anything to do with this disease of rice or whether it is the result only of dampness.

That the explanation so likely in theory, appears only too evident in fact, and further experiment may complete the chain of evidence showing this to be the true cause of beri-beri.

The most important point is the vitality of the organism and calls for a better method of cooking rice in large institutions.

P. 43

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12

Beriberi on the Isthmus of Panama.

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Captain, Assistant Surgeon.
U. S. ARMY.

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Reprinted from The Journal of the American Medical Association, January, 1907.

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BERIBERI ON THE ISTHMUS OF PANAMA.*

IRA A. SHIMER, M.D.
Captain, Assistant Surgeon.
U. S. ARMY.

39 Whitehall
N. Y. C

It is not the purpose of this paper to give any new information on the etiology of beriberi. The subject has been extensively investigated by Pekelharing and Winkler, Manson, Wright and the Japanese school, and germs have been isolated, which, it is claimed, are the cause of the disease. These claims, however, have not been substantiated. Beriberi has been attributed to faulty diet, to various forms of intestinal parasites, to exposure to the elements, and, finally, in absence of definite knowledge, to malaria. The consensus of opinion is that beriberi is a place infection and probably of microbic origin; it is immaterial whether, as Manson states, the germ is located in the soil of infected spots and produces a toxin which gains entrance to the body and causes the symptoms characteristic of the disease, or whether the germ itself gains access to the body and there generates a toxin which produces the disease.

The knowledge gained by the Japanese during the late war toward the prevention of beriberi by the changed dietary proves little or nothing, because, as pointed out by Scheube, late professor of the Medical School at Tokio, so many hygienic reforms were put into effect at the same time, which by themselves would tend to improve the general health. Beriberi attacks persons living in damp, ill-ventilated and overcrowded buildings; in this locality it has been especially noted that it is common among the pearl fishers. With the knowledge gained during the past few years relative to the transmission of disease by the mosquito, is it not extremely probable that this insect plays an important part in the transmission of this disease? To sum up, the causative agent of beriberi has not been determined, nor has the mode of the transmission of the infection been demonstrated.

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* Published under the Imprimatur of the American Society of Tropical Medicine.

Beriberi is a specific form of multiple peripheral neuritis, with frequent involvement of the cardiopneumogastric system, the latter manifesting itself by both functional and organic (dilatation of the right side of the heart) disturbances.

TYPES.

The varieties of beriberi on the Isthmus differ in no way from those generally described, namely, 1, the dry, atrophic or paraplegic type; 2, the wet or dropsical type; 3, the mixed forms. It is proposed to give an outline of the symptoms of each of these varieties.

1. The Dry, Atrophic or Paraplegic Type.—Probably the earliest symptoms of beriberi cases is the pain felt in the epigastrium. This is often present for several months before other symptoms appear. The patient first notices a gradual loss of power in the legs, followed by atrophy of the calves of the legs, with loss of sensation over the front of the tibiæ, the sides of the thighs, and very frequently of the finger tips and of areas on the arms. Manipulation of the muscles is painful. Patellar reflex and ankle clonus are usually absent. The gait in these cases is ataxic; there is marked toe-drop, causing the patient when walking to raise the foot a considerable distance above the ground and to bring it down with a characteristic flop. These patients use various sorts of devices to assist themselves in progression, and when walking with a support place as much of their weight as possible on this support. Examination of the cardiac area shows a greater or lesser degree of pericardial effusion; the heart sounds overlap each other; there is a general cardiac irritability; throbbing of the carotids and pulsating movements in the jugular vein.

2. The Wet or Dropsical Type.—In appearance this type differs entirely from the preceding. The face of the patient is puffy and heavy; the lips cyanosed, and the trunk and members of the body are edematous. The urine is scanty and dark colored, of high specific gravity, but in the majority of uncomplicated cases contains no albumin. The edema is firmer than that of nephritis. It may be localized and disappear from day to day. Hydrothorax and hydroperitoneum are frequently present. There is rarely any edema of the scrotum. The heart shows the same conditions as in the atrophic cases. The patellar reflexes are absent and the disturbances of sensation are the same as in the atrophic cases.

3. *The Mixed Types.*—In this type of case there is some edema, especially of the feet, about the flanks, over the buttocks and sternum and in the region of the neck. The patellar reflexes are absent; there are areas of anesthesia over the tibiæ. The cardiac symptoms are the same as in the types described above. The general health of these patients is not affected. The appetite is good; the tongue clean, and unless there are complications there is no fever.

SYMPTOMATOLOGY.

In reviewing the symptoms of beriberi, the paralyses and atrophy of the voluntary muscles do not play an important part as to the life of the patient. The real danger depends on the amount of involvement of the cardiopneumogastric innervation. Patients who are up and around one day and apparently doing well suddenly collapse and are dead the following day. This is pointed out by Manson as probably due to a chain of circumstances; to degeneration of the heart muscle following nerve destruction; to imperfect systole in consequence of an interrupted nerve supply and to obstruction to capillary circulation in consequence of vasomotor paresis in the pulmonary and in the general circulation. When the dilatation once begins, it tends to increase of its own accord; the more the heart dilates the more difficult it is for it to contract. Finally, the distension is so great that it fails to contract altogether and death is inevitable. Therefore, the prognosis in beriberi should always be guarded, for the case that is apparently mild may suddenly develop serious symptoms.

BERIBERI ON THE ISTHMUS.

The records of physicians who have practiced on the Isthmus for years show that beriberi was unknown here prior to the year 1887. The death registers of the French Canal Company began in January, 1881; those of the city of Panama in November, 1883. There are no records of deaths from beriberi in either of these registers prior to 1887. In that year the canal company imported a number of Chinese and African contract laborers. The first death from beriberi among the canal employés occurred in July, 1887. The first recorded death from beriberi in the city of Panama occurred in December, 1887, five months after the first death among the laborers of the French company. After its first appearance its spread on the Isthmus was rapid, especially among the poorer classes and among the colored races.

The description of beriberi given above refers to the ordinary uncomplicated cases. Almost all the cases which have come under observation in the hospitals on the Isthmus show numerous divergences from the above, due to the multiplicity of complications. A local practitioner of Panama informed me that 450 severe cases of beriberi which he treated began acutely with chills and fever. The fever was of a malarial type and responded promptly to quinin. After the fever subsided and the patients attempted to go about their usual vocations, they showed the typical symptoms of beriberi. As stated above, probably the earliest symptom of beriberi is the epigastric pain. If this is not severe, it would probably not be noticed by the patient unless his attention was afterward called to it by the physician. Hence the opinion prevailing among local practitioners that beriberi is of malarial origin. To illustrate further the complications in beriberics, it is proposed to add a series of cases, taken from the records of Ancon Hospital, giving the clinical histories and pathologic data, and showing beriberi complicated by malarial fever, ankylostomiasis, chronic nephritis of various types and locomotor ataxia.

CASE REPORTS.

Case 1.—G. M., of Martinique, was admitted to Ancon Hospital Jan. 6, 1906. Patient complained of pains in legs and thighs: of burning sensations in the feet; calves of legs were painful on slightest pressure; patellar reflexes were absent. Albumin was noted in the urine January 25. The patient died Jan. 30, 1906, at 4:10 a. m.

Autopsy—Autopsy at 8 a. m. gave the following findings:

Heart: Right heart considerably dilated. Intestinal tract: Mucosa anemic; no indication of hemorrhage; intestine contained round worms, whip worms, and *Ankylostoma americana*. Kidneys: Enlarged, soft and greatly congested. Spleen: Five times normal size: extremely firm; fibrous elements increased: stroma dark brown color; stained smears show estivo-autumnal parasites. Bone marrow: Estivo-autumnal parasites present.

Comparing the clinical with the pathologic data in this case, the former justified the diagnosis of beriberi, the latter the diagnosis of acute parenchymatous nephritis; of ankylostomiasis and of malarial fever, estivo-autumnal.

Case 2.—J.T., Barbadian, was admitted to Ancon Hospital Jan. 22, 1906; died Jan. 22, 1906.

Clinical Diagnosis.—Bronchopneumonia.

Pathologic Notes.—All subcutaneous tissues were edematous. Right pleural cavity contained about 200 c.c. amber colored fluid; pulmonary edema marked; pericardium contained about 150 c.c. straw colored fluid. Heart was acutely dilated. Spleen five times normal size; deeply pigmented stroma, with miliary patches scattered uniformly throughout. Smear showed many pigmented malarial parasites of the estivo-autumnal type. Kidneys acutely congested. Intestinal tract: Ankylostoma and round worms.

Pathologic Diagnosis.—Acute beriberi, estivo-autumnal and malarial fever, and ankylostomiasis.

In this case the clinical symptoms justified the diagnosis of bronchopneumonia; the pathologic, the diagnosis of acute beriberi, malarial fever and ankylostomiasis.

Case 3.—F. H., Panaman, aged 23, was admitted to Ancon Hospital Nov. 14, 1905; died Nov. 15, 1905, 8:30 p. m.

Clinical Notes.—Illness began with pain in stomach and weakness in legs; patient was unable to walk; there was numbness of legs and hands; ankles were swollen; there was tenderness over tibiæ and thighs; abdomen was tender; morning temperature, 98; evening temperature, 100; pulse, 100 to 124; respiration, 24; ankylostoma ova present.

Pathologic Notes.—Left pleural cavity contained 100 c.c. of fluid; pericardium 50 c.c. of fluid. Kidneys were congested. Intestines: In mid-portion of small intestine were many *Uncinaria americana,* both male and female; duodenum, stomach and remainder of intestinal tract normal. Spleen: Small number of pigmented malarial parasites.

This represents an almost uncomplicated case of beriberi of the dropsical type. The evening temperature of this patient was probably due to the ankylostomiasis, as there were no malarial parasites demonstrable in the peripheral circulation.

Case 4.—Ancon Hospital. Patient showed patellar reflexes absent; marked pain in the calves of the legs on pressure; general anasarca.

Pathologic Notes.—Hydropericardium; hydrothorax and chronic nephritis.

Case 5.—W. J., aged 54, Jamaican, on isthmus 20 years, was admitted to Ancon Hospital March 2, 1905; died March 26,

1905. Patient first noticed swelling of feet, which increased rapidly, extending up the legs; there was considerable amount of pain in calves of legs and knees; patient complained of shortness of breath in walking; temperature normal; pulse, 136; respirations, 28 to 36.

Pathologic Notes.—Peritoneal cavity contained about 200 c.c. amber colored fluid; pericardial cavity 60 c.c. amber colored fluid. Kidneys: Right kidney, weight 2 ounces; cortex, 7 m.m.; pyramids pale: capsule stripped with difficulty in places; right kidney as above.

Pathologic Diagnosis.—Chronic diffuse nephritis.

Case 6.—A. G., Colombian, colored, was admitted to Ancon Hospital Jan. 31, 1905; died Feb. 10, 1905. Illness began one and one-half months prior to admission, with swelling in the feet; there was pain in the muscles of the extremities, difficulty in walking, and dyspnea.

Examination.—Edema of the ankles and feet; apex-beat diffuse; epigastric pulsation with double mitral murmur; pulse 130: great muscular weakness. especially in legs; wasting of calves of legs and thighs; hand grasp weakened; gait ataxic; patient raised legs with difficulty: there was pain on deep pressure of the calves; knee jerk was diminished: there were no anesthetic areas. Urine showed large quantities of albumin; examination of stools showed the presence of ankylostoma.

Diagnosis.—Beriberi and chronic interstitial nephritis.

Pathologic Notes.—Left kidney was very small: capsule adherent in strips; cortex very thin; minute hemorrhage in pelvis; right kidney one-half normal size and same as above. Heart greatly dilated. Stomach, mucosa showed minute pin point hemorrhages: also the first eight inches of duodenum showed marked injection and numerous pin-head elevations, whitish in color. Pin-point hemorrhages were very numerous.

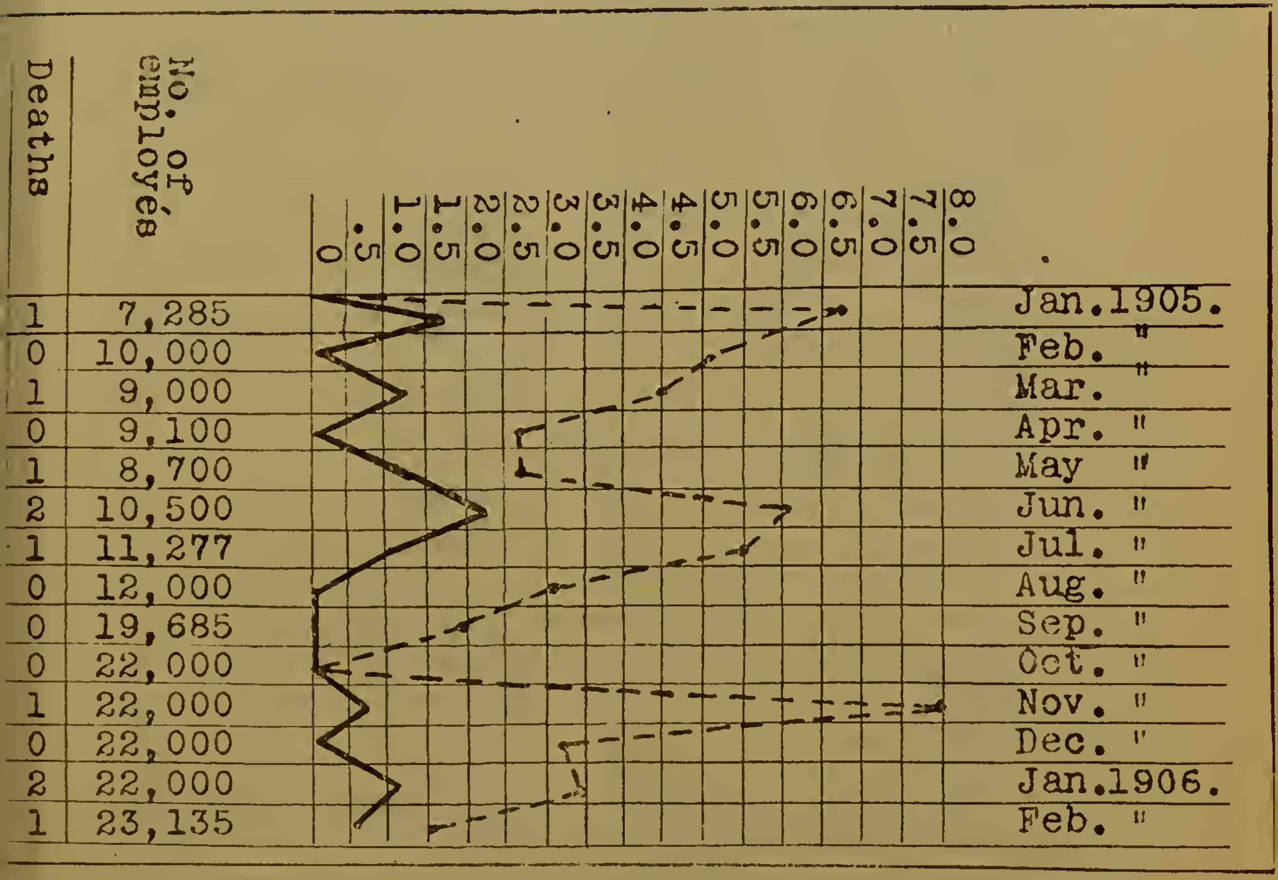
Case 7.—J. E., aged 46, American, had used alcohol in considerable amounts for a number of years; he denied venereal history. One month ago patient noticed swelling of ankles. This was followed by loss of power in the legs and irritability of the heart when walking rapidly.

Examination.—Patellar reflexes were absent; ankle clonus was absent; there was pain in calves of legs on pressure; slight anesthesia over tibiæ; Romberg symptom was positive; slight incoördination in movements: Argyle-Robertson symptom was negative.

Cases of this character are very often misleading and it is difficult to make diagnoses between incipient locomotor ataxia and beriberi. It is believed, however, that the absence of the Argyle-Robertson pupil would justify the diagnosis of beriberi, which was made in this case. The subsequent history has confirmed the diagnosis of beriberi.

In autopsies which show symptoms of beriberi and of ankylostomiasis, examination of the intestines very often shows in the duodenum around the worm a large red patch about 4 cm. in diameter. This is superficial and might tend to give one an idea of some pathologic condition due to disease and not to the presence of the worm.

In several deaths from acute beriberi the mucous membrane of the stomach and the upper part of the small intestine was found hyperemic and at some places hemorrhagic. One postmortem showed innumerable white spots, the size of a pinhead, scattered over the mucous surface of the duodenum.



Deaths	No. of employes	
1	7,285	Jan.1905.
0	10,000	Feb. "
1	9,000	Mar. "
0	9,100	Apr. "
1	8,700	May "
2	10,500	Jun. "
1	11,277	Jul. "
0	12,000	Aug. "
0	19,685	Sep. "
0	22,000	Oct. "
1	22,000	Nov. "
0	22,000	Dec. "
2	22,000	Jan.1906.
1	23,135	Feb. "

TREATMENT.

As the majority of beriberi cases originate in damp, ill-ventilated and overcrowded habitations, the first essential in the treatment is removal from the probable source of infection. Patients should be placed in a dry locality in well-ventilated rooms. It is customary in Panama to send such patients as can afford the expense to the Island of Taboga. The climate of this island, situated 12 miles from Panama in the Bay of Panama, has long been noted for the beneficial results to patients who have had attacks of beriberi and malarial fever. Patients should be well fed, and bulky articles of diet should be eliminated. The medicinal treatment is entirely symptomatic. Digitalis and strophanthus for the heart, with general tonics and massage and electricity are indicated.

ANALYSIS OF CASES.

In examining the records of cases treated in Isthmian Canal hospitals, 112 cases of beriberi are tabulated. Of this number, 106 patients were males and 6 females. There were 14 deaths among those treated. The admissions to hospital occurred as follows:

1904.	
September	1
October	2
November	0
December	2
1905.	
January	7
February	7
March	6
April	5
May	4
1905.	
June	9
July	7
August	8
September	5
October	1
November	21
December	14
1906.	
January	9
February	4

Ages at admission ranged as follows:

10 to 20	16
20 to 30	45
30 to 40	24
40 to 50	11
50 to 60	8
60 to 70	4
Not stated	4

The sources of admission were as follows:

City of Panama and vicinity	77
City of Colon and vicinity	14
Culebra	9
Matachin	2
Empire	3
Pedro Miguel	2
Gorgona	1
Paraiso	1
Bohio	1
Bas Obispo	2

The length of time on the Isthmus outside of the cities of Colon and Panama was as follows:

From Culebra: Five patients had been on the Isthmus upward of ten years. The remaining four had been on the Isthus, respectively, one month, two months, and two about five months each.

The Matachin patients, upward of thirty years.

The Empire patients, five months, one and one-half months and two months.

The Pedro Miguel patients, one seven years, the other four months.

The Bas Obispo patients, one sixteen years and one six months.

The Gorgona, Paraiso and Bohio patients, unknown.

Of the above 112 cases treated in the Isthmian Canal Commission hospitals, 64 patients were employés of the Isthmian Canal Commission. Among these 64 there were 10 deaths. The morbidity was greatest in the month of November, 1905, when with a total of 22,000 laborers there were 15 admissions to hospital, giving a morbidity rate of slightly more than 8 per 1,000 per annum.

The mortality rate among commission employés was greatest in the month of June, 1905. In this month there were 10,500 laborers on the rolls. Five beriberi patients were admitted to the hospital, of whom 2 died, giving a mortality rate of 2.3 per 1,000 per annum. The reader is referred to the chart hereto attached, giving the morbidity rate and death curves for employés of the Isthmian Canal Commission from January, 1905, to February, 1906, inclusive.

In looking over the records of the French Canal Company it is impossible to find the morbidity rate for beriberi. The mortality rate for the French company in November, 1887, was 22½ per 1,000 per annum. Deaths from beriberi were very rare among the employés of the French company during the years 1890, 1891, 1892, 1893, 1894, 1895 and 1896. In 1897, however, the death rate rose to the alarming figures of 54 per 1,000 per annum. This occurred in the month of May. Comparing this with the mortality rate for yellow fever among the employés of the French company, we find that their highest mortality rate from the latter disease was in 1882, and reached 5.8 per 1,000 per annum, or slightly more than 1/10 that of beriberi. To sum up, the highest death rate from beriberi under the Isthmian Canal Commission has been 2.3 per 1,000 per annum, and under the French company 54 per 1,000 per annum.

Deaths from beriberi in the Isthmian Canal Commission by nationality:

Colombia	18
Dominica	1
Panama	14
Jamaica	7
Africa	1
Spain	1
St. Lucia	1
Mexico	3
Costa Rica	1
Grenada	1
France	2
Barbadoes	3
Martinique	6
Guadaloupe	1
British Honduras	1
Germany	1
Fortune Island	1
Total	64

Deaths from beriberi in the French company by nationality:

China	65
Africa	127
West Indies	25
Colombia	7
Cuba	1
America	1
England	2
France	2
Belgium	1
Total	231

BERIBERI IN THE CITY OF PANAMA.

As stated before, the first death from beriberi in the city of Panama of which there is record occurred in December, 1887. Since that time there has been no year in which there have not been deaths from this cause. For the past 8 years, however, there has been a decided increase in the number of deaths. It is impossible to compare the mortality rate with the morbidity rate, as these cases have heretofore not been reported. The highest mortality rate occurs with great regularity in the last 3 months of each year, namely, October, November and December. Beginning with the year 1899 the mortality rate has risen from 4.5 per 1,000 per annum to 5 in 1900, 7 in 1902 and 11 in 1903. It dropped to 8.5 in 1904 and again rose to 11 per 1,000 per annum in 1905. There were 559 deaths from beriberi reported in Panama from 1887 to 1905, inclusive, distributed by nationality as follows:

China	114	Chile	1
West Indies	36	Venezuela	1
Colombia (Panama)	368	Nicaragua	1
Mexico	9	Cuba	1
Ecuador	5	America	3
Peru	4	France	3
Costa Rica	4	Spain	2
Salvador	3	Italy	1
Guatamela	2	Sweden	1

As an example of place infection of beriberi in Panama, the Bovedas prison may be cited. The ground floor of this building has been used as a prison for many years. It is built of stone, is poorly ventilated and at times overcrowded. The cases originating in this prison by months are as follows:

BERIBERI IN BOVEDAS PRISON.

Year.	Month.	No. of cases.	No. of prisoners.
1904	April	1	Not known.
	May	0	6
	June	0	23
	July	1	31
	August	1	47
	September	2	53
	October	2	58
	November	2	59
	December	2	77
1905	January	0	67
	February	0	63
	March	3	45
	April	0	49
	May	1	51
	June	4	47
	July	3	67
	August	3	68
	September	1	65
	October	3	59
	November	3	56
	December	0	69
1906	January	0	75
	February	0	75
	March	0	69

Late in October, 1905, the prisoners were transferred from the prison proper into another portion of the same building, with conditions practically the same as before. Refernce to the table above shows that after the first month there were no new cases.

The question naturally arises that with the presence of beriberi in Panama, and the appearance of sporadic cases in the Zone, what are the chances of an outbreak of this disease among the laborers of the commission, the same as occurred under the French régime? It is believed that the improved sanitary conditions, better habitations, the feeding of the laborers by the commission, this insuring a better dietary, and our increased knowledge of the management of tropical disease, will all tend to render an outbreak of this disease improbable.[1]

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[1] I am indebted to Dr. Samuel T. Darling, pathologist, Acon Hospital, for valuable pathologic data.

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Notes on Beri-Beri

As observed in the Malay Peninsula
from 1882 to 1888

BY

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(From the Transactions of the British Medical Association Meeting, held at Leeds, 1889.)

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L MEDICINE

BERI-BERI.

Beri-beri.—The attempts at the solution of the derivation of this term are very numerous, and in some cases ingenious. The term Beri-beri is stated by some to be derived from the Malay word for sheep, viz. biri-biri, on account of persons so affected walking like sheep, but my experience of upwards of ten years amongst the Malays does not bear this out. In the native States of the Malay Peninsula the disease is universally known as "Sâkit kaki bĕngkak," and only is the term "beri-beri" used by "travelled" Malays—Javanese and other immigrants to the Peninsula.

The term "Beri-beri" is fast becoming universally adopted, and in a few years this disease will only be known by this name—a name which bears out its meaning, being derived from the Sanscrit "bhara," a weight, the repetition simply intensifying the meaning of the word, and every patient so affected describing the principal symptoms as a great weight in his chest, legs, or arms as the case may be.

Beri-beri appears in the Malay Peninsula both in an endemic and epidemic form, where it attacks principally the Chinese coolies working in the tin mines; but this disease is not peculiar to them alone, as it affects other nationalities as well, and men, women, and children.

The majority of cases that I have dealt with were males averaging from 19 to 30 years of age, this being the age of the majority of immigrant coolies. Seldom is an old man affected, and still more so are boys, and when they are, are readily cured. Women not being so much exposed to the causes which bring on this disease, are consequently not so much affected, although I have seen numerous cases amongst the lower prostitute classes of Chinese.

The mines are not what we in England understand by the term. Those of the Malay Peninsula are merely excavations in the valleys, varying from 12 to 40 feet deep, sometimes more, and varying in extent according to the stanniferous deposits. The ore is found in the form of what is known as stream tin, in the alluvial deposits, and is separated from the sand and other foreign matter very much in the same manner as gold is, in sluice boxes. The coolie houses are situated on the edge of or close to this excavation. Although there is as a rule plenty of running water, still sanitary requirements of any kind are not carried out. The

Chinese coolie is a difficult man to deal with: his prejudices are very strong as well as his superstitions, and they have an inherent spirit to evade the laws especially of sanitation. But a great deal can be done (although somewhat arduous in a new country, and that country a tropical one) to improve matters, and for this purpose I have personally visited the different mining coolie sheds throughout the States of Perak and Selangor from time to time.

I cannot do better than relate here a few incidents of a visit to the mines of Kinta, in Perak, by myself in June, 1882.

At Goping, during 1882, I visited a mine where there were 3,000 Chinese working tin, and out of this number 300 had died, since January, of beri-beri, showing a death rate from beri-beri alone in six months of 10 per cent. Here I also learned that it had only been known within the last two years, and that from 8 to 9 per cent. of Chinese coolies fresh from China take beri-beri. I was also informed that sinkhehs (i.e. labourers from China brought under contract) are more susceptible than the free coolie is to beri-beri, while the Towkheys or headmen are entirely free from this affection. This alone points to (1) poor living and (2) poor accommodation, (3) poor clothing and (4) exposure, as some of the causes of this dread disease.

In this same district I visited mines worked by Malays, and although their mines are on a very much smaller scale than the Chinese, still I did not come across a single case of beri-beri in them. This on the other hand points to (1) better living and (2) cleanliness of body and (3) cleanliness of habitation, together with the (4) sanitary requirements of the Mahomedan laws, as preventatives of beri-beri.

In the Ipok district I learned that upwards of 37 per cent. of miners had died from beri-beri for the first half-year; and in this district, as in the Goping district, the "sinkhehs" were the most numerous, while the headmen were not affected at all by beri-beri. Sporadic cases had occurred in this district in former years, but never before 1882 was it epidemic.

In the Kinding district I saw in one mine alone 10 cases of bere-beri, all being coolies over five years from China, and strange to say, not one sinkheh or new-comer suffered. As all these men could speak Malay, I was able to converse with them, and they assured me that their illness commenced by repeated attacks of fever, ending in the swelling of abdomen and legs which came on during the hot and dry weather.

In the Papan district, all the cases of beri-beri that I saw were what is known as "dry" beri-beri, the Malays naming it "sâkit bêring anging," and here the natives informed me that it attacks old as well as new residenters, and that the cause of it appearing in an epidemic form was due to the wet weather at the beginning of the year (1882), followed by hot and dry weather. The natives in this district also informed me that women as well

d in the legs,

as men suffered from this disease; and while I was there a young Malay woman, who had had three children, died of beri-beri. In this district, a number of women wash tin ore from the rivers, and consequently suffer more from exposure. The Towkheys or Chinese headmen in this district, as in others, do not suffer from beri-beri, this again showing that beri-beri can be avoided by better living and better habitation than the ordinary coolie can get, and providing ordinary precautions against exposure and other debilitating causes.

It is exceedingly difficult to see a case of beri-beri from the beginning of the disease, the majority of cases presenting themselves for treatment when they are "in extremis," but the following is a brief account of the onset as observed by me. There is first of all a feeling of malaise followed by weakness and rheumatic-like pains in the knee joints with a dull continuous pain round the region of the stomach: the pain in the knees passes downwards and backwards to the feet, followed by a feeling of numbness and sometimes swelling of the legs and feet with œdema, and presenting all the appearances of Bright's disease: the pain in the stomach increases and the abdomen may swell and become tense from ascites. Sometimes there may be no swelling of the legs, but an emaciation and atrophy of the muscles with loss of power, and in those cases it generally affects the arms as well. The pulse is soft and compressible, at times hard and jerky: there is a thrill over the region of the heart and strong pulsations in the sternal notch, neck and temples: hœmic murmurs are very distinct and there are moist crepitations at the base of both lungs: knee and elbow jerks are usually absent. Below the elbow there is a numb dead feeling, more marked in the fingers, and the hands are cold with more or less loss of grasping power. The peculiar gait is well marked, the foot being thrown forward with a jerk and raised considerably, the toes coming to the ground first. There is generally an inclination to fall on closing the eyes and placing the feet together. As a rule, there is no loss of sensation, but the patient generally describes the ground or floor as being a cushion or carpet under his feet. Sometimes there may be aphasia, and the patient in advanced stages is only able to converse in a husky whisper. There is a feeling of suffocation on lying down, which is relieved by a pillow: the appetite is generally bad, and the bowels are constipated, with clay-coloured stools, but sometimes severe diarrhœa sets in. The patient may die soon after the attack, or he may linger on for five or six months, rarely longer: he dies suddenly, and in great pain, of a burning character, in the chest and abdomen. He recovers his voice, and with an anxious countenance shouts out for help up to the last moment.

The Chinese and Malays believe that a person once having been attacked by beri-beri, never gets permanently cured.

[illegible] Hartwards [illegible]
Beek ~~[illegible]~~ Conclude, but never had an opportunity
examining any cases of the [illegible]

On the examination of the blood of 100 typical cases of beri-beri, the red discs were found to be pale and few in number, and only in one case was I able to find a micro-organism and that of the filaria type. On one occasion, I inadvertently and unknown to myself at the time, was innoculated at a post-mortem examination of a beri-beri case, the result the next day being a puffiness over the cheek bones and swelling of the eyelids, ankles, and feet, with a feeling of great heaviness of the latter, and general malaise, all of which passed away in about eight days, the original wound healing rapidly: the only medicinal precautions taken being a dose of Epsom salts in the mornings and 3 grs. of quinine before meals, followed in three days by a course of strychnine and iron.

In the Report on Beri-beri in Atjeh, 1886, Drs. Cornelissen and Sugenaya state that "Beri-beri must be considered a contagious disease induced by some micro-organism." The following facts, which have come under my own observation, tend to the same view being taken.

In the first ward that was built (1882) of the General Hospital, Kwala Lumpor, Selângor, I observed, during 1883, one wooden bed on which when patients were placed, no matter with what complaint they were admitted, were certain to develop symptoms of beri-beri, and such a state of things existed until I had to have the bed destroyed, and shortly afterwards the ward was pulled down and the woodwork burned.* In the new wards, where plank and trestle beds were used and great cleanliness enforced, this was not noticed.

Again in the old Police station (1882) at Kôtah Bharu in Perak, where out of necessity convicts suffering from beri-beri were detained, there was a strong able-bodied Malay man of the name of "Lis" arrested and placed in this lock-up, who shortly afterwards developed beri-beri, and was very far advanced in this disease when I last saw him. This lock-up† consisted of one small association ward protected above by a thatched roof and surrounded by upright round bars of wood or jungle rollers.

In the old Gaol at Kwala Lumpor, Selângor, which was similar in structure, although much larger, to the afore-mentioned Lock-up,—and which has since been pulled down, wood-work destroyed, and site changed,‡—things were getting so bad that a convict after being confined in this gaol for over three months was almost certain to develop symptoms of beri-beri: there being two marked exceptions, one being the Malay chief-warder and his wife, who lived in the gaol enclosure for 8 years, but they occupied a detached room, and who up to the present are well and healthy; the other being a Chinese lunatic, who out of choice slept in one of the association wards and fed either with the convicts or the beri-beri cases in this gaol for a period of 8 years, when he was removed to Singapore Lunatic Asylum, after which I lost sight of him.

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* This was the subject of a special report to the British Resident, Mr. F. A. Swettenham, who after minute enquiries gave orders that the ward and beds should be burned whenever other accommodation was provided.

† Shortly afterwards destroyed and Kôtah Bharu abandoned.

‡ On the representation of Mr. Swettenham, British Resident.

For example, I may here relate one case of a Chinese convict who had not been a month in this gaol, and who on commitment was strong and healthy, was admitted to the Gaol Hospital on 11th January, 1883, complaining of pains in the chest, stomach, knee joints and bones of the legs, with a feeling of weakness in them and weight of the feet with a general malaise. He was about 35 years of age, of middle height and strongly built, and to all appearance well nourished: the eyes and face were slightly puffy, the ankles were slightly swollen and pitted on pressure: the feet were cold to the touch: on walking there was an inability to point the toes except with a jerk, and the characteristic beri-beri gait was present. The abdomen and chest were slightly distended, and dark ropy blood oozed from the skin on being scratched: there was a thrill over the precordia, especially towards the apex. A muffled murmur was heard at the apex and base of the heart: there were marked pulsations in the sternal notch and base of the neck and temples: pulse small, jerky, and irregular: moist crepitations at base of lungs: the bowels were constipated; urine presented oxalates but no albumen: no rise of temperature was observed. The autopsy presented the lungs pressed backwards and collapsed; they were not crepitant at the edges and were full of pigment; the pericardium contained 20 ozs. of green fluid; the right side of heart was full of black blood, and left side firmly contracted: the tricusped valves had fibrinous deposits on them, while the semilunar were normal: the liver was much enlarged, extending to the edges of the opposite floating ribs, with a nutmeg appearance on section: the spleen was greatly enlarged and brittle; kidneys appeared normal. No anchylostoma were found in the intestines, but three ascarides were found in the colon: fæces were hard, impacted and of a clay colour.

NOTE.—This man did not complain before the 11th January, and died suddenly on the morning of 14th January. Shortly before death there was marked meteorism. No history of malarial cachexia known, but probably there was.

Parisites found in the intestines of Beri-beri cases:—

The post-mortem examination of the intestines of 100 Sinkhehs (or new comers under contract from China) at the Pauper Hospital, Kwala Lumpor, during 1887–88, revealed the following:—

Anchylostoma duodenale were present in	80
No parasites were found in . .	20

but the stomach and intestines were in a state of extensive catarrh.

Distoma Crassum (or *Sinense*)* with *Anchylostoma* were present in 1 case.†

Ascaris Lumbricoides with *Anchylostoma* were found in 20 cases.

Wherever the worms were found, the neighbouring mucous membranes were very much eroded, the size varying from a pin's head to that of a shilling. The erosions took a crescentic and oval shape, not round. No parasites were found in the stomach, the duodenum, cœcum, and small intestines being the parts most infected. The colons although ulcerated or eroded, no *Anchylostoma* were found in them, but *Ascaris Lumbricoides* were present.

When I took over charge of the Hospitals of Selângor, in 1882, there were three Chinese beri-beri cases under treatment. The first case that was reported was on 14th February, 1882. On the 16th February, a Malay Policeman was affected, and admitted to Hospital. At this time, a Malay Police-sergeant died at his own house, from all the symptoms described, of beri-beri.

In April, 1882, 35 beri-beri cases were in Hospital. It then seemed to spread with great rapidity all over the country, and especially in the mines, and cholera broke out in Perak and Selangor.

During the same month (April) all the cattle commenced to die off, of what appeared and which was reported as diarrhœa, but the symptoms appeared to me to be more of a typhoid character. I examined the Government bullocks that died, and found in the paunch, gullet, nose, windpipe, and lungs, numerous larvæ similar in appearance to the Macaco worm of South America. On further examination I took it to be Cuterebra noxialis.

Beri-beri had been known to exist in an endemic form in the mines for two years previous to this epidemic. The natives informed me that they believed the cause was a flood which occurred in December, 1881, followed by heavy rains.

In December, 1880, the rainfall was	11·12	inches.
January, 1881, ,, ,, ,,	3·81	,,
February, 1882, ,, ,, ,,	8·04	,,
	22·97	Total inches.
While in December, 1881, it was	13·88	
January, 1882, ,,	11·08	
February, 1882, ,,	6·60	
	31·56	Total inches.

This flood and extra rainfall were most probably factors in beri-beri taking an epidemic form, but it must be remembered that at this time the Malay Native States were being opened up to the outer world, and were attracting numbers of Chinese, as tin miners, also Javanese and other nationalities of the Malay Archipelago : and this immigration has gone on increasing until 1887, when 20,000 immigrants entered the State, and 30,274 passengers by steamers were passed inwards by the Medical Department ; but unfortunately beri-beri has also gone on increasing, until, in 1887, 1,585 were treated in the Hospitals of the State, and of those 69 per cent. were discharged cured during the year.

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* Now in the Museum of Leeds Medical School, and with Sir William Turner, University of Edinburgh.

† The case was reported at this Meeting, and the specimens of *Distoma* shown.

I will now give the analyses of 100 cases of beri-beri, as they presented on admission to the Government Hospitals of Selângor (1885) :—

Nationalities.

Chinese	99
Javanese	1
	100

Occupation.

90 were tin miners
1 was a fireman at the mines
2 were charcoal burners
5 were railway coolies
2 were road coolies
100

Duration of Disease (previous to admission).

6	— 10 days
4	— 15 ,,
5	— 20 ,,
23	— 1 month
3	— 1½ months
11	— 2 ,,
13	— 3 ,,
6	— 4 ,,
7	— 5 ,,
4	— 6 ,,
3	— 7 ,,
3	— 8 ,,
3	— 11 ,,
4	— 12 ,,
3	— 15 ,,
3	— 3 years
100	

Condition (on admission).

(*a*) 25 could walk with a stick
27 could walk a little with a stick
15 could walk very little with a stick
33 could not walk at all, being carried into Hospital
100

(*b*) 52 were dropsical
35 were not dropsical
13 had œdema of ankles
100

(*c*) 19 had weakness of the wrist-joint alone and loss of grasping power
29 had weakness of the wrist, elbow, and knee joints, and loss of grasping power
52 presented no marked weakness of joints or loss of grasping power
100

24 complained of no pains, other symptoms present
16 „ of lumbar pains only
12 „ „ lumbar and girdle pains
17 „ „ lumbar, girdle, and joint pains
10 „ „ pains in shoulder and knees only
11 „ „ „ calves of the legs only
10 „ „ joint pains only
100

Percussion on Spine.

51 pain on percussion, with great pain in two cases over the lower dorsal and upper lumbar region
49 no pain at all
100

Reflex.

(*a*) 20 the cremastor reflex absent
25 „ „ „ present
55 were not examined
100

(*b*) 24 elbow and knee jerk absent
35 „ „ „ not well marked
13 „ absent (only)
12 knee „ „
16 both reflexes were present
100

Staggering on closing eyes and placing feet together.

34 staggering
25 not evident
41 not examined
100

Syphilis.

43 history of syphilis
57 no history of syphilis
100

Urine (passed during the first 12 hours).

6 passed from 20 to 30 ozs., colour pale straw, sp. gr. 1020, no sugar, no albumen, urates and phosphates, 40 grs. solid matter.

7 passed 18 ozs., colour light straw, no albumen, urates and phosphates in abundance.

8 passed 4 ozs., colour pale straw, 84 grs. solid matter, no albumen, oxalates and epithelial cells present.

9 no urine passed.

10 passed 5 ozs., colour smoky amber, sp. gr. 1030, acid reaction, no albumen.

27 passed 25 ozs., colour clear amber, acid reaction, sp. gr. 1032, no albumen, traces of sugar.

33 passed 11 ozs., colour clear amber, reaction acid, sp. gr. 1020, solid matter 40 grs., traces of sugar, no albumen.

100

The peculiar beri-beri gait was well marked in all the above cases.

The following are brief notes of a few Beri-beri cases treated in the Pauper Hospital, Kwala Lumpor, Selângor, during 1888, for which I am indebted to Mr. Chief-Apothecary Focnander and Mr. Apothecary Keun :—

Case 1.—Sou Phah. A Chinese admitted to Hospital 19th Feb., 1888, with Beri-beri, aged 28. Duration of disease, 2 months.

History.—A Sinkheh tin miner: arrived three months ago from China. After a residence of 3 months at the mines got ill: was able to walk to hospital.

Treatment.—Was put on tonic treatment of iron and digitalis, and arsenic: no improvement until May, when he was put on santonin and castor oil. On 12th May, passed one ascaris; 13th, three ascarides; 14th, three ascarides; 16th, two ascarides. He was then put on iron and digitalis until 27th July, when he was discharged cured.

Note.—No other parasites were found, although the stools were closely examined and passed through muslin. His diet consisted of bananas, rice, and beans, with beef, milk, and three ounces of gin in the day. The urine was acid.

Case 2.—Ah Sam. Chinese, æt. 28. Admitted 21st Feb., 1888. Diagnosis, wet beri-beri. Duration of disease, 3 months.

History.—A Sinkheh tin miner, from China, after being three months at the mine got sick and unable to work. When admitted to hospital was able to walk very little: the elbow and knee jerks were absent.

Treatment.—Diuretic. No improvement until 9th May, when he was put on santonin and castor oil for three days: passed 8 ascarides: was then put on iron and strychnine with digitalis at intervals. He continued to improve, and was discharged cured on 21st June, 1888. Diet was generous, with three ounces of gin in the day.

Case 3.—Chang Sam. Chinese, æt. 29. Admitted 9th March. Diagnosis, dry beri-beri. Duration of disease, 30 days.

On admission, was unable to walk, elbow and knee jerk absent: urine strongly acid.

History.—A Sinkheh tin miner, 14 months from China: got sick after being two months at the mine.

Treatment.—Iron and quinine; santonin and castor oil; and then iron and strychnine.

Note.—Was able to walk on 5th May; great improvement on 12th June; elbow jerk present and knee absent on 10th July. Was discharged 23rd July cured, both elbow and knee jerk were present.

Diet was generous: no gin given: no parasites were noticed in stools.

Case 4.—Chang Sieng, Chinese, æt. 24. Admitted 19th March, 1888. Diagnosis, beri-beri. Duration of disease, 10 days.

History.—A Sinkheh tin miner: got ill after being three months at the mine, and was unable to walk.

Treatment.—Iron and strychnine: no improvement. On 31st March was put on male fern; then arsenic and quinine. 9th May, put on santonin and castor oil for three days, as prescribed by Kuhenmeister: on the 12th May passed three ascarides: was then put on tonic treatment, such as iron and quassia, iron and strychnine. 10th June, could walk a little; 4th July, could walk fairly well; 30th July, discharged cured.

Case 5.—Lee Soo Lang. Chinese, æt. 25. Admitted 24th Mar., 1888. Diagnosis, dry beri-beri. Duration of disease, 20 days.

On admission, was unable to walk: elbow and knee jerk absent: loss of grasping power.

Treatment.—Iron and quinine. 9th May, santonin and castor oil; no parasites passed. 21st May, iron and strychnine. 2nd June, could walk a little. 12th June, could walk pretty well. 26th June, was discharged: grasping power returned, also elbow and knee jerk.

Case 6.—Seng Ong. Chinese, æt. 28. Admitted 25th March, 1888. Tin miner. Diagnosis, wet beri-beri. Duration of disease, 2 months.

On admission, was able to walk very little; knee jerk absent; bowels constipated.

Treatment.—Tonics, digitalis and gin. 9th May, santonin and castor oil, followed by tonic treatment. 23rd May, diarrhœa set in, from which he never recovered. Died 21st June, 1888.

Section.—No parasites found; masses of round clay-coloured fæces in gut; great effusion in pericardium.

Case 7.—Ah Paw. Chinese, æt. 32. Admitted 27th March, 1888. Tin miner. Diagnosis, dry beri-beri, tendo reflex absent. Duration of disease, 1 month.

On admission, was unable to walk. *History.*—Had had syphilis.

Treatment.—Iron and quinine; santonin and castor oil; followed by iron and quassia. On 12th June, put on iron and strychnine; 18th June, was able to walk with a stick; 2nd July, was able to walk without a stick; 16th July, could walk pretty well; 21st July, discharged cured.

Case 8.—Ah Hoon. Chinese, æt. 42. Admitted 27th March, 1888. Tin miner. Diagnosis, wet beri-beri. Duration of disease, 1 month.

On admission, was unable to walk; weakness of wrists; knee and elbow jerks absent; urine strongly acid.

Treatment.—Diuretic; no improvement. 12th May, santonin and castor oil; 14th, passed three ascarides; 15th, passed two ascarides; feet commenced to swell; tonics. 5th June, was able to walk very little; put on iron and strychnine; 12th June, could walk pretty well. 23rd June, discharged cured.

Case 9.—Wang ben. Chinese, æt. 24. Admitted 30th March, 1888. Tin miner. Diagnosis, dry beri-beri. Duration of disease, 1 month.

On admission, was unable to walk; knee and elbow jerk absent; loss of grasping power; urine acid reaction.

Treatment.—Tonics and digitalis. 9th May, santonin and castor oil, followed by iron and quassia. 2nd June, was able to walk with a stick. 30th June, was able to walk well. Tendo reflexes being absent, he was put on iron and strychnine until 30th July, when he was discharged cured.

History.—He was a Sinkheh tin miner, fresh from China, and was two months in the mine when attacked by beri-beri.

Case 10.—Yap Yang. Chinese, æt. 22. Admitted 7th April, 1888. Fireman. Diagnosis, dry beri-beri. Duration of disease, 3 months.

On admission, unable to walk, weakness of wrists.

Treatment.—Iron and strychnine; 9th May, santonin and castor oil; 13th, iron and quassia; 4th June, could walk a little; 12th, greatly improved; 25th June, discharged cured.

Case 11.—Thien Toon. Chinese, æt. 24. Admitted 14th April, 1889. Tin miner. Diagnosis, wet beri-beri (anasarca). Duration of disease, 1 month.

On admission, unable to walk; weakness of wrists; tendo reflex absent (knee and elbow); bowels constipated.

History.—A Sinkheh tin miner from China; was three months in the mine and from China when he got sick.

Treatment.—Diuretic; 9th May, santonin and castor oil; 14th, passed four ascarides; 23rd, able to walk a little; 10th June, could walk pretty well, and the anasarca much reduced; 21st June, great improvement, could walk well; was put on iron and strychnine on 16th June; 26th July, was discharged cured.

Case 12.—Liew Lay Shin, Chinese, æt. 35. Admitted 10th April, 1888. Tin miner. Diagnosis, dry beri-beri. Duration of disease, 15 days.

On admission, was able to walk very little; constipated; elbow and knee jerk absent.

History.—A Sinkheh on a tobacco estate in Delhi, Sumatra, where after a residence of four months had an attack of beri-beri; was in hospital for a month, when he was discharged; came to Kwala Lumpor and worked in a tin mine for 5 months, when he had a recurrence of his former illness.

Treatment.—Tonics; 9th May, santonin and castor oil, and was quite unable to walk after this. 26th May, iron and strychnine given; 29th June, able to walk with sticks; 2nd July, tendo reflexes returning; 12th, able to walk without sticks; 19th, could walk pretty well; 27th, could walk very well, tendo reflexes not well marked; 28th, discharged.

Case 13.—Ng Kim, Chinese, æt. 22. Admitted 15th April, 1888. Tin miner. Diagnosis, dry beri-beri. Duration of disease, 20 days.

On admission, was unable to walk; urine very acid; tendo reflexes absent.

History.—Had been in the State upwards of 4 years, and had worked in the mines for 3 years and 7 months, when he got sick.

Treatment.—Iod. of potassium; 9th May, santonin and castor oil; 10th June, iron and strychnine; 12th, able to walk a little; 7th July, could walk pretty well; 23rd July, discharged cured.

Case 14.—Kan Yoon, Chinese, æt. 25. Admitted 26th April, 1888. Tin miner. Diagnosis, dry beri-beri. Duration of disease, 1 month.

On admission, unable to walk; tendo reflexes absent; bowels constipated; urine very acid.

History.—A Chinese Sinkheh 7 months from China; got beri-beri after being six months in the mine; had had syphilis.

Treatment.—21st May, was put on strychnine and iron; 2nd June, could walk a little; 23rd, could walk pretty well; 10th July, could walk very well, tendo reflexes still absent; 21st July, discharged cured. Reflexes marked.

CASE 15.—CHIN KIAN, Chinese, æt. 40. Admitted 6th May, 1888. Tin miner. Diagnosis, dry beri-beri. Duration of disease, 20 days.

On admission, could walk very little; tendo reflexes absent; urine acid; bowels constipated.

History.—This man had been in the Malay Peninsula many years, and had been a miner, a road and shop coolie. He had been in the mines for the last year, when he got ill, and being unable to work or walk came to hospital.

Treatment.—9th May, santonin and castor oil; 15th, passed numerous ascarides in the form of a knotted mass; 16th May, put on iron and strychnine, after which he improved, and was discharged 21st June, 1888.

CASE 16.—CHIT YON, Chinese, æt. 27. Admitted 20th May, 1888. Tin miner. Diagnosis, dry beri-beri. Duration of disease, 1 year.

On admission, could walk very little; elbow and knee jerks absent; constipated.

History.—This was the second time he had had beri-beri; this second attack came on two months after working in the mine.

Treatment.—21st May, calomel and senna, until the bowels were moved freely: soup diet only. 22nd May, thymol grs. xxx. given in the early morning, and repeated at intervals of two hours, for three times. No anchyloshoma or other parasites were passed; was then put on iron and calumba. 18th June, could walk pretty well; 25th June, right knee and elbow jerk present; 18th July, tendo reflexes present, and could walk well; 24th July, discharged cured.

CASE 17.—AH SANG, Chinese, æt. 34. Admitted 29th June, 1888. Tin miner. Diagnosis, wet beri-beri. Duration of disease, 2 months.

On admission, was able to walk very little with the assistance of sticks; tendo reflexes were absent.

History.—He was a free coolie, and had been working in a mine for six months. He had been upwards of 10 years in this country (i.e. since he left China); had been in the mine four months, when he got sick, and was treated by Chinese doctors at the mine until he came to hospital.

Treatment.—30th June, was put on diuretic mixture; 7th July, got iron and strychnine; 21st July, was able to move about without sticks; 27th, could walk very well, reflexes returning; 30th July, discharged cured.

CASE 18.—YANG LAI, Chinese, æt. 35. Admitted 16th July. Tin miner. Diagnosis, wet beri-beri. Duration of disease, 2 months.

On admission, was able to walk a little.

History.—Had been in the country 5 years, and had always worked in the mines.

Treatment.—Was put on santonin and castor oil; no parasites were detected. 19th July, iron and quassia; 24th, iron and quinine; 30th July, discharged cured.

Case 19.—Book Seak, Chinese, æt. 30. Admitted 21st July, 1888. Tin miner. Diagnosis, dry beri-beri. Duration of disease, 1 month.

On admission, was able to walk a little; tendo reflexes were absent; urine very acid.

History.—Been in this country upwards of five years; came to hospital whenever he was unable to work.

Treatment.—Iron and strychnine. Discharged at his own request on 30th July, saying he was going back to work in the mine. He was then quite able to walk, but the beri-beri gait was slightly noticeable.

Remarks.—In reference to the afore-mentioned cases, the beri-beri gait was well marked in all those who could walk. Albumen was absent from the urine, which was in a number of cases strongly acid. The presence of the elbow and knee jerks in a number of cases was peculiar. The usefulness of ahthelmintics where internal parasites are suspected. The usefulness of iron and strychnine tonics. Malarial cachexia was present in them all.

A. W. S.

Royal Colonial Institute,
Northumberland Avenue, London, W.C.,
1st August, 1889.

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II.—Contribución al estudio de la función renal en los pacientes.
III.—Sugestiones acerca de la patogenia de los edemas.

TRABAJO PRESENTADO AL 6º CONGRESO MÉDICO LATINO-AMERICANO

REUNIDO EN LA HABANA DEL 19 AL 26
DE NOVIEMBRE DE 1922

POR

A. J. VALENZUELA, M. D., PH. B.
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Ex-Profesor Sustituto de Clínica Interna en la misma Facultad,
Médico del Hospital General,
Miembro de la Asociación Escuela de Medicina,
Miembro de la S. Médico Quirúrgica del Guayas,
Ex-Sec. de la Sección Médica del 1er. Congreso Médico Ecuatoriano,
Ex-Subsecretario de Gobierno, Higiene i Sanidad
Officier d' Academie.
Ex-Medecin au service de la Mission Geodésique Française de l' Equateur.

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BERIBERI

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I

El Beriberi ha existido seguramente desde tiempo inmemorial en el Ecuador, pero pasaba desapercibido, por cuanto la mayor parte de los casos ocurrian entre los peones i montuvios de las plantaciones de caña de azúcar, de arroz i de cacao, donde generalmente no hai médicos i sabida es la animadversión con que antes miraba esta clase de gente al hospital i careciendo de recursos, preferían dejarse morir en los campos, antes que venir a la ciudad para asistirse en el hospital. Esta es la razón para que, como dejamos dicho, pasaran inapercibidos estos casos con la etiqueta de consunción, hidropesía, i de caquexia palúdica. Cosa igual pasaba con la ankylostomiasis. Su distribución geográfica está limitada á las provincias de Los Ríos i parte de las del Guayas, i El Oro i en Manabí desde el cabo San Francisco hasta el Norte i en toda la provincia de Esmeraldas. También existe en el Oriente.

Hace veinte años nadie hablaba de beriberi en el país. Los primeros casos que me fué dado estudiar fueron en la tripulación del buque de guerra colombiano «Bogotá» que procedente de Buenaventura vino a Guayaquil poco después de la secesión de Panamá. El diez i nueve por ciento de los hombres de abordo estaba atacado de una enfermedad consistente en edema de los miembros inferiores; en cinco o seis de ellos el edema estaba generalizado i constituía un verdadero anasarca. Pálidos, anemiados, todos ellos; algunos incapaces para tenerse en pié, con una postración única, pulso muy frecuente, facies angustiosa; sensibilidad de las masas musculares del muslo i de la pierna; reflejos patelares, en unos abolidos en otros, normales. Las condiciones generales de higiene i en especial de alimentación, no eran satisfactorias. No había médico a bordo, ni farmacéutico.

Aunque solo conocía de beriberi las descripciones de Sir Patrick Manson i de Le Dantec, no me fué difícil hacer el diagnóstico. Una vez mejorada la alimentación i las condiciones higiénicas de la marinería, i bajo la acción de una terapéutica adecuada, todos los pacientes mejoraron i cuando la «Bogotá» zarpó del puerto toda su tripulación pasó revista sobre la cubierta.

La experiencia adquirida me fué mui útil i mas tarde, tanto en mi servicio de medicina de mujeres en el Hospital General, como en la práctica urbana, he visto i diagnosticado muchos casos de beriberi,algunos de los cuales he utilizado para hacer conocer la enfermedad a mis alumnos. Como es natural, al principio, este diagnóstico hecho por un facultativo novel i sin ninguna reputación, era mirada con cierto escepticismo i no se admitía para esos enfermos otro diagnóstico que el de cardiacos asistólicos, cardiorenales, i polineuríticos mas o menos alcohólicos, mas o menos palúdicos; al fin, como la verdad acaba siempre por abrirse paso, al fin llegó el convencimiento al ánimo de todos. Espinoza Tamayo hizo preparaciones histológicas de los nervios pneumogástico i femoral de una enferma fallecida en mi sala, con la forma hidrópica, i quedó comprobada la degeneración nerviosa, lo que vino a disipar todas las dudas:

Desde entonces todo el mundo diagnostica beriberi i el conocimiento de la enfermedad se ha divulgado aún entre los profanos, especialmente con motivo de la campaña de Esmeraldas, donde la afección tomó carácter epidémico no solo entre el elemento militar,sinó también en la población civil, cuya alimentación i condiciones higiénicas, se resintieron profundamente a consecuencia de la aglomeración de personas i del prolongado sitio.

Para juzgar de la frecuencia de la enfermedad i de la mortalidad que produce, insertamos aquí los siguientes datos sacados de la Estadística de Enfermedades noticiables de la Dirección de Sanidad.

BERIBERI EN LA CIUDAD DE GUAYAQUIL

1921	Asistidos	Defunciones
Noviembre	8	0
Diciembre	6	0
1922		
Enero	7	1
Febrero	3	0
Marzo	4	0
Abril	7	1
Mayo	5	0
Junio	4	1
Julio	6	1
Agosto	6	1
	56	5

Lo que dá una totalidad de nueve por ciento sobre la morbilidad de beriberi, que se aproxima a la cifra de diez y trece por ciento que produce en otras partes.

El porcentaje de defunciones sobre la mortalidad total en la ciudad de Guayaquil, puede observarse en el siguiente cuadro, cuyos datos son tomados de la Estadística de los Cementerios que publica anualmente la Junta de Beneficencia Municipal.

Años	Total de defunciones	Defunciones por Beriberi	Parálisis	Polinculitis
1911	3421	0	10	7
1912	5508	0	15	0
1913	4231	7	8	7
1914	3823	4	8	19
1915	4191	16	18	15
1916	3877	0	8	4
1917	3887	2	7	8
1918	4435	4	10	6
1919	4787	8	11	4
1920	5255	2	11	1
1921	4131	4	16	7
	47.526	47	122	78

De donde se vé que el beriberi produce el uno por mil anual de mortalidad. Hemos insertado las cifras de parálisis i de polineuritis para que sirvan de comparación.

Por regla general la forma seca del beriberi domina entre nosotros por su frecuencia a la forma hidrópica; si bien es cierto que casi todos los casos tienen edema pretibial, ello no constituye síntoma dominante para caracterizar la enfermedad, de modo que para ser justos diremos que las formas mixtas son las que más frecuentemente se ven i oportunamente i convenientemente tratados, como hemos visto, su mortalidad es reducida, pues las cifras anteriores corresponden en gran parte a las formas agudas que felizmente son poco frecuentes, porque son pocos los que escapan de ellas con vida. Los que fallecen es generalmente en medio de sufrimientos horribles, conservando casi siempre hasta el último instante, la integridad de sus facultades mentales, la muerte sobreviene ya por parálisis del corazón mas o menos brusca, o en aplanamiento progresivo, yá por asfixia producida por diafragmoplegía i por parálisis de los demás músculos respiratorios. Uno de los casos más graves que vimos salvar fué el del distinguido hombre público, artista i escritor notable Don Luis A. Martínez quien en su novela «A la Costa» hace de la enfermedad una descripción tan real i naturalista como la que hace de la viruela Emilio Zola en una de sus magistrales novelas.

Los trastornos mentales son rarísimos, sin embargo hemos visto dos casos, uno de los cuales terminó por la muerte, en un apreciabilísimo joven estudiante de Bachillerato, que tomó la enfermedad en la hacienda de sus padres, cercana a Puebloviejo en la provincia de Los Ríos, en el cual, simultáneamente con los trastornos paralíticos, se desarrolló el triste e impresionante cuadro de la psicosis polineurítica de Korsakoff: antecedentes hereditarios, nerviosos, por una parte, i la dedicación al estudio, sin compensación en su desenvolvimiento físico, por otra, fueron sin duda las causas predisponentes que originaron tal síndrome en este caso.

Las formas frustradas, ambulatorias, son también comunes, no solo en el campo sino también en la ciudad de Guayaquil i otras del litoral.

II

Siempre nos llamó la atención la falta de síntomas urémicos en el beriberi, aun en pacientes graves, moribundos, con disfagia, que impedía toda alimentación; la falta de albuminuria que es verdaderamente escepcional; la falta de cilinduria que no hemos encontrado jamás; el carácter del edema que sin ser propiamente duro como el del mixedema, difiere del edema de los brighticos hidropígenos, por ser algo mas duro i no dejarse deprimir con el dedo sinó es con cierta resistencia; por ir acompañado algunas veces de hipersensibilidad, sin haber signos inflamatorios locales i por su falta de predilección hacia ciertas zonas facilmente edematizables como el escroto i los párpados, en que el tejido conjuntivo es más laxo.

Desde los trabajos de la Escuela Francesa moderna, el estudio de la fisiología renal ha sufrido un progreso grande. Durante muchos años se discutió si el riñón era un filtro o una glándula, tal discusión no existe yá; como tal obra el riñón cuando forma ácido hipurico por síntesis de la glicocola i del ácido benzoico; cuando transforma la bilirrubina en urobilina i en fin cuando produce urocromo. Pero la función glandular no consiste solamente en eliminar sustancias que no preexisten en la sangre, en cuyo caso dicha función glandular sería muy restringida, sino que como tal debemos considerar tambien el poder colectivo del riñón para concentrar los productos eliminados, a tal punto que los hallamos en la orina a una concentración cien veces mayor que aquella en que se encuentran en la sangre lo que constituye un proceso vital importantísimo, que, está sometido a leyes matemáticas fijadas por Ambard. Esta sin duda la parte mas importante de la función glandular, merced a ella se verifica la excrecion de sustancias que es preciso eliminar, para mantener constante la composición de la sangre, de ese medio interior como lo llamaba Claudio Bernard, condición indispensable para la armoniosa vitalidad de la economía.

Según Ambard la eliminación renal es de tres clases: por efracción por difusión i por secreción. En cuanto a las sustancias eliminadas hai que dividirlas en dos grupos: sustancias puramente excrementiciales, que se eliminan en alta concentración, que no son necesarias para la vida, i sustancias por el contrario indispensables a la economía, que solo necesita el organismo eliminar cuando su taza sanguínea sobrepasa ciertos límites: las primeras se filtran entre tanto halla de ellas vestigios siquiera en la sangre, es decir, sin límite o umbral de eliminación; las segundas se filtran solo mientras su concentración sanguínea tiene un exceso sobre la taza vital necesaria. Estas son las sustancias que tienen umbral de excreción.

Todo este estudio, con el bello mecanismo de la movilidad de los umbrales i de las leyes de Ambard que rigen la eliminación renal i el estudio de la concentración máxima de las diversas sustancias eliminadas, que es mutuamente isoiónica, es una de las mas grandes conquistas de la biología moderna.

Tantos progresos en la fisiología normal del riñón debían forzozamente influir benéficamente en nuestros conocimientos sobre las nefritis, i efectivamente hemos asistido a una reforma, una revolución en el concepto i clasificación de las mismas.

La división antigua de las nefritis era a la vez histológica i clínica,pero su denominación era exclusivamente histológica. Nadie había añadido ni modificado en nada el concepto i la nomenclatura de Bright, el padre, el fundador, de la patología renal. Las nefritis se dividían en nefritis epiteliales, intersticiales i mixtas. El gran riñon blanco i el pequeño riñon rojo continuaban siendo el prototipo de dos procesos distintos. La nefritis epitelial era nefritis con albuminuria i con edemas;la nefritis intersticial no tenía albuminuria ni edemas, sino poliuria, hipertensión vascular, hipertrofia ventricular izquierda, anorexia i caquexia seca. La nefritis mixta era un complejo de las dos anteriores, la epitelial i la intersticial.

Magnus, Vidal, Ambard i Papin fueron los leaderes de esta revolución triunfadora. No solo se ha cambiado la clasificación, lo que tendría un valor teórico i didáctico solamente, se ha renovado el concepto del funcionalismo fisiológico, sinó que también la fisiopatología renal mejor interpretada, permite el mas racional tratamiento dietético i medicamentoso del que se deriva un enorme beneficio para los desventurados pacientes: Se ha demostrado que las células renales no son como las células cerebrales, vírgenes encerradas en su caja de marfil, incapaces de reproducirse, sino que están dotadas del poder de reproducirse, de llegar a la hipertrofia compensatriz, que conocen i practican el lema «renovarse o morir». Las nefritis crónicas son pues suceptibles de cura, siempre que sepamos dar con la causa que las entretiene i que una vez conocida podamos ponerla fuera de combate,

La nueva nomenclatura se basa sobre la diferenciación de las secreciones renales descubierta por Widal i sus discípulos: nefritis hidrópigenas, nefritis uremigenas, nefritis albuminúricas simples, nefritis hipertensivas i todas las combinaciones resultantes de las diversas asociaciones de estas formas fundamentales o tipos puros.

La obra de Ambard i sus colaboradores, que la clínica confirma con la misma matematicidad de sus fórmulas, i que acabará por imponerse al criterio médico universal, permite ya graduar la intensidad de las nefritis, midiendo la capacidad funcional del riñón, permitiendo al médico práctico medir a su vez la cantidad i calidad de la alimentación conveniente a los enfermos sometidos a su cuidado; permitiendo al cirujano una seguridad respecto a la conveniencia posible de una anestesia, de una intervención quirúrgica, con una fijeza, que el simple índice urémico está mui lejos de provisionar.

Widal probó que de todas las sustancias eliminadas por el riñón, el Cl Na es la única hidrópigena, aunque bien pueden darse casos de retención clorurada sin edemas i sin aumento de peso, lo que ha sido demostrado por Snapper en la sangre de los pneumónicos, cuya retención clorurada es una de las más agudas e intensas que conoce la Patología, siendo de notarse que dicha retención no se efectúa en el plasma, merced a una retención de H_2O concomitante, sino a una afinidad patológica de los hematies por Cl Na, que se encuentra sólidamente fijado en ellos ¿Pasa lo mismo en todos los demás tejidos de la economía, o solo en el parénquima pulmonar flegmasiado? El autor no lo dice ni tampoco si se trata de un fenómeno tóxico o de una defensa bienhechora:

La aplicación de todos estos datos modernos al estudio de la función renal en el beriberi, debía ser harto provechosa por la interpretación fisiopatológica de sus edemas, de su dispnea, cuanto preñadas de conclusiones útiles en relación con el diagnóstico, la dietética i el tratamiento de las víctimas de esa enfermedad.

Había observado anteriormente que el régimen aclorurado no tiene influencia apreciable sobre los edemas en la forma hidrópica del beriberi; había observado que entre los casos de beriberi naval que vemos entre los tripulantes de las embarcaciones de vela que hacen el cabotaje en la costa, en quienes la carne salada i el pescado salado o crudo, del mar, forma la parte más importante de la alimentación, no existe la forma hidrópica con más frecuencia, ni con más intensidad que la forma seca, siendo entre ellos como entre los montuvios la forma mixta la más frecuente.

Estos eran bastantes datos para juzgar clínicamente que los edemas en el beriberi no reconocen por causa una eliminación clorurada insuficiente, pero tal conclusión necesitaba de un estudio prolijo de la función renal con determinación del balance clorurado por medio de la administración progresivamente creciente de Cl Na.

El índice urémico i la constante urosecretoria de Ambard nos permitirían apreciar el papel de la retención uréica en la producción de ciertos otros síntomas como la dispnea, por ejemplo.

Vamos a exponer la historia clínica, i los resultados obtenidos en esta observación, para la cual hemos tenido la valiosa cooperación de nuestro Jefe de Laboratorio Dr. Francisco Rojas.

V. P. 23 años, de raza mestiza, blanca i etiópica, de oficio agricultor, natural de Guayaquil, reside alternativamente en la ciudad i en el campo. Anteriormente ha gozado por regla general de buena salud, i entonces su permanencia habitual era la hacienda, i Babahoyo, a donde iba, por un día o dos, cada quince días, aproximadamente. Mui trabajador, de costumbres higiénicas, no bebía licores, ni chicha, ni cerveza. Sus antecedentes familiares nada dicen de interés: su padre tampoco era alcohólico.

Entra en mi clínica en anasarca i en brazos agenos, siendo de notar que el no puede tenerse en pie, a pesar de que la dispnea de que se queja no es permanente, 18 respiraciones al minuto, en decúbito dorsal, existe una taquicardia moderada (en reposo noventa i cuatro pulsaciones), a la palpación, el pulso parece pequeño, pero la presión arterial al Pachón es 13 Mx; i 8 Mn; el reflejo óculo cardiaco hace bajar las pulsaciones a cincuenta i ocho por minuto. El edema es generalizado, pero sí se puede notar que los párpados no están especialmente edematizados, que el líquido en la cavidad peritoneal, si lo hai, es en mui pequeña cantidad i que el escroto no está edematoso. Los reflejos aquilianos i patelares están abolidos; puede caminar apoyándose en otra persona, pero no puede pararse solo i para ello hai materialmente que levantarlo tomándolo de los brazos. Al apretar las masas musculares del muslo i de la pantorrilla había una sensibilidad exagerada. Pulmones absolutamente normales.

Dice que su enfermedad ha comenzado hace un año por accesos de sofocación caracterizados por violentas palpitaciones, angustia epigástrica, con sensación de constricción en la parte inferior del tórax, dolor en la región de la nuca, imposibilidad absoluta para tenerse en pie, insomnio, vómitos, constipación mui rebelde; en los momentos álgidos de estas crisis llegó a perder el conocimiento alguna vez, pero nunca tuvo relajación de esfínteres. Habitualmente sufre de elevación del vientre después de las comidas. Estos ataques tienen una duración variable de una a dos horas, terminando por sudores copiosos. Después de cada una de estas crisis el pulso ha quedado cada vez más frecuente, i ha sido visible el aumento de los edemas, en las extremidades inferiores, i adormecimiento de ellas, así como también en las manos, edemas que han ido progresando hasta llegar al anasarca. El peso del paciente en estas condiciones oscila al rededor de 215 libras.

Estos ataques de sofocación, vecinos de la asfixia se verificaban en sucesión, casi siempre durante la noche, eran rebeldes a toda medicación; en cambio mejoraban visiblemente con el cambio de residencia.

Diversos facultativos lo han atendido, diversas medicaciones ha seguido.... últimamente le habían hecho una sangría de algo más de medio litro i después se le había hecho una inyección de suero Hayem (Cl Na endovenosa 7 ‰) i con esta medicación no ha experimentado ni mejoría ni empeoramiento apreciable, lo cual era una sugestión más de que sus riñones eran aptos para eliminar un exceso considerable de Cl Na ingresado bruscamente en su sangre.

El diagnóstico seguido hasta allí parece haber sido el de nefritis: así lo demuestra el régimen sin carne y declorurado a que había estado sometido el paciente, quien venía bien documentado con diversos exámenes de laboratorio, como vamos a ver:

ABRIL 30—1918. Examen completo de orina

Cantidad	— 950 c. c.	Ext. seco 100	22,—	grs.	°/oo	Urobilina	—vestigios
Aspecto	—turbio	Mat. orgánica	17,—	,,	,,	Indol	,,
Color	—anaranjado	Mat. minerales	5.—	,,	,,	Escatol	,,
Olor	—sui géneris	Acidez (Ac. Ox.)	0,52	,,	,,	Albúmina	NO HAY
Reacción	—ácida	Urea	16,13	,,	,,	Peptonas	,,
Densidad	—1015	C. xanto-úricos	0,52	,,	,,	Albumosas	,,
Sedimento	—abundante	Cloruros	0,35	,,	,,	Glucosa	,,
		Fosfatos	1,74	,,	,,	Acetona	,,
Sedimento:		Sulfatos	2,86	,,	,,	Hemoglobina	,,
Abundantes crist. de urato de soda, escasos de ac. úrico, bacterias.						Pig. biliares	,,

El presente examen se verificó estando el paciente en régimen declorurado; como se ve, lo único que llama la atención es la cifra de 0,35 grs %⁰ de ClNa que si bien no es la cantidad contenida en un litro de leche (1,50), etc, que habitualmente se ingiere en este régimen, debe tomarse en cuenta la cantidad eliminada por el sudor, etc. Es mui importante la ausencia de albúmina además de la de otros elementos anormales. La cifra de urea guarda relación normal con la de ac. fosfórico.

MAYO 1º 1918—Examen citológico de sangre:

Polinucleares neutrófilos	78,15 %
,, acidofilos	9.63 ,,
,, basófilos	0,00 ,,
Formas de transición	0.74 ,,
Linfocitos	9,63 ,,
Grandes mononucleares	1,85 ,,

Lijera elevación de la cifra de polinucleares neutrófilos i acidófilos, disminución de linfocitos.

No hai hematozoario de Laverán.

MAYO 1º 1918—Materias fecales-Examen microscópico.

Escasos tricomonas, algunos glóbulos blancos, pocas células intestinales, cristales de fosfato amónico magnesiano, fibras vejetales i células de almidón.

MAYO 1º 1919—Esputos-Análisis bacteriológico.

Micrococus catarralis, neumococos, escasos glóbulos blancos, células epiteliales alteradas, levaduras, hongos i espirilos banales.

En los dos exámenes útlimos no hai, pues, algo notable.

MAYO 31 1918—Examen completo de orina.

Cantidad	740 c. c.	Ext. seco 100	31,00 grs °/oo	Urobilina	Vestigios
Aspecto	límpido	Mat. orgánicas	24,00 ,,	Indican	,,
Color	ambarino	Mat. minerales	7,00 ,,	Excatoxilo	,,
Olor	sui generis	Acidez(ac.oxal)	0,99 ,,	Albúmina	NO HAI
Reacción	ácida	Urea	22,95 ,,	Albumosas	,,
Densidad	1019	C. xanto-úricos	0,52 ,,	Peptonas	,,
Sedimento	mui escaso	Cloruros	vestigios	Mucina	,,
		Fosfatos	3,74 ,,	Glucosa	,,
		Sulfatos	2,96 ,,	Acetona	,,
				Hemoglobina	,,
				Pig. biliares	,,

Sedimento:

Cristales de ácido úrico, fosfato tricálcico, urato de soda, bacterias banales.

El anterior examen también fué practicado durante el régimen declorurado. Hai aumento relativo de la cantidad de urea i ac. fosfórico pero guardando siempre su relación. Los vestigios de urobilina, indol i escatol son debidos á la constipación que acompaña a cada ataque, cada uno de los cuales motiva su respectivo examen de orina.

JUNIO 21 1918—Examen completo de orina

Cantidad	960 c. c.	Ext. seco a 100	21,00 °/oo	Urobilina	vestigios
Aspecto	turbio	Mat. orgánicas	9,00 ,,	Indol	exceso
Color	anaranjado	Mat. minerales	12.00 ,,	Escatol	vestigios
Olor	Amoniacal	Acidez(ac.oxal)		Albumina	NO HAI
Reacción	alcalina	Urea	8.06 ,,	Albumosas	,,
Densidad	1012	C. xanto-úricos	0,46 ,,	Peptonas	,,
Sedimento	escaso	Cloruros	7,15 ,,	Glucosa	,,
		Fosfatos	2,02 ,,	Acetona	,,
		Sulfatos	2,68 ,,	Hemoglobina	,,
				Pig. biliares	,,
				Mucina	,,

Sedimento: fosfato amónico-magnesiano, urato de soda, urato de amoniaco i ácido úrico; células epiteliales alteradas i levaduras.

Este examen se practicó durante un régimen hipo-azoado é hipo clorurado NO HAI ALBUMINA.

Al ingresar a la clínica i después del examen clínico que hemos expuesto, pensamos ya que no podía tratarse de una nefritis, sinó de un caso de beriberi de forma hidrópica i para comparar con los análisis anteriores dispusimos se hiciera el siguiente

Examen de orina completo, bajo régimen lacteo desde nueve días antes.

Cantidad	630	Ext. seco a 100	34,03	‰	Urobilina	NO HAI
Aspecto	turbio	Mat. Orgánicas	30,65	,,	Indol	,,
Color	ambarino	Mat. Minerales	33,38	,,	Escatol	,,
Olor	amonical	Reac. alcalina		,,	Albumina	,,
Densidad	1029	Urea	27,20	,,	Albumosas	,,
Sedimento	notables	C.Xanto úricos	1,36	,,	Peptonas	,,
		Cloruros	0,58	,,	Glucosa	,,
		Fosfatos	0,60	,,	Acetona	,,
		Nitrógeno total	14,36	,,	Hemoglobina	,,
		Sulfatos		,,	Pig. i sales	
				,,	biliares	,,

Sedimento no hai cilindros: cristales de fosfato amónico magnesiano.

Fecha: Diciembre 26 de 1918.

La víspera, el estudio comparativo de la urea en la sangre i en la orina, nos había dado el siguiente resultado:

DICIEMBRE 25 1918.—Régimen lácteo, inyección diaria de 0,006 grs. de sulfato de estricnina 8 días antes de la siguiente prueba:

Constante ureica de Ambard

Nombre V. P. Edad 23 años. Peso 62. 4 Kilos. Temperatura 37°. c.

ORINA: Vejiga evacuada a las 2 horas 22 minutos 30 segundos.
Orina recogida a las 4 horas 16 minutos 30 segundos.
Duración de la prueba 1 hora 54 minutos.
Volumen obtenido durante la prueba 50 cc.
Volumen referido a 24 horas 631 cc.
(c) Concentración de urea, por litro 23,95 grs.
(D) Caudal de urea, referido a 24 horas, 15,12 grs. Constante: K=0,07 normal.
SANGRE: (Ur) Cantidad de Urea por litro 0,253 grs.

$$\frac{\text{Ur.}}{\sqrt{D\times\frac{70}{P}\times}\sqrt{\frac{C}{25}}}=K;\qquad\frac{0.253}{\sqrt{15{,}12\frac{70}{62{,}4}}\sqrt{\frac{23.95}{25}}}=K0.06$$

No hai albúmina.

Volumen en 24 horas, desde 3 días antes de la prueba, 750 cc.

Llama la atención la baja cifra de urea sanguínea simultánea de la alta concentración (C) a que ha sido emitida la orina, con un caudal (D) considerable de urea, referido a 24 horas. Por esta circunstancia se ha podido efectuar la determinación del coeficiente ureo-secretorio en el presente caso, como se podría en cualquier sujeto normal bajo las condiciones de oliguria, como éste. En efecto; sabido es que la concentración máxima a que un sujeto sano emite la urea en la orina llega a 55 ‰. En el presente caso que solo hai que eliminar 15,12 grs. referido a 24 horas, pudo hacerse hasta con un volumen de orina menor de 500 cc. ref. a 24 h. Por otra parte el criterio más fácil i mui exacto acerca de la eliminación renal ureica lo suministra la cifra de concentración ureica urinaria, en estado olígurico, ya que la concentración máxima disminuye a medida que la lesión renal avanza; de donde la necesidad de la poliuria del brightico, el que luego se hace azotémico *"por un mecanismo compensador que pone a los riñones en un estado de presión uréica"*.

Basta, pues, mirar detenidamente el resultado obtenido i examinar las condiciones en que se practicó la determinación de la constante ureo-secretoria para creer en la óptima permeabilidad renal ureica en este sujeto.

Permeabilidad renal al cloruro de sodio

Más sensible aun que la ingestión salina simple i la prueba de la hidratación, por la balanza, la determinación del ritmo de retención i eliminación del cloruro de sodio, etc. indica de la manera más fiel i exacta el valor renal respecto a la excreción salina.

He aquí el resultado obtenido con nuestro sujeto:

FECHAS	Cloruros Ingeridos	Volumen	Cloruros eliminados	
			por litros	en 24 horas
Enero 1-1919	1,50	668	1,75	1,17
,, 2-1919	1,50	684	1,87	1,28
,, 3-1919	1,50	800	1,28	1.05
,, 4-1919	1,50	663	1,93	1,28
,, 5-1919	8,00	749	5,85	4,38
,, 6-1919	18,00	1000	11,70	11,70
,, 7-1919	7,00	500	13,45	6,72
,, 8-1919	1,50	500	8,77	4,38
,, 9-1919	1,50	225	10,53	2,36
,, 10-1919	1,50	250	5,26	1,32
,, 11-1919	1,50	425	6,43	2,73
,, 12-1919	1,50	800	2,92	2,33
,, 13-1919	1.50	731	1,75	1,28
,, 14-1919	1,50	1273	1,28	1,63

El organismo normal si se lo somete a régimen declorurado i si en el tiempo en que ha logrado establecer el equilibrio de entradas i salidas de cloruro alimenticio se le hace ingerir por tres días una cantidad de 10 grs. de Cl Na, diaria, verifica una retención de 10 a 16 grs. de sal con 1 a 2 kilos de aumento de peso merced a un ritmo en escalones; pero al tercer día se establece el equilibrio clorurado. Si en este estado se le somete nuevamente a régimen declorurado se observará la eliminación de la sal retenida bajo un ritmo en escalones semejantes al de la retención.

En los brighticos puede ocurrir:

1°—Si la permeabilidad está disminuida, el ritmo en escalones se prolonga, la duración de la retención no será 3 días como en sujeto normal sinó 5, 6, 7, etc. días, siendo esta retención mayor i si es posible aumentando la hidratación.

2°—Si la permeabilidad fuese mui disminuída o casi abolida, el ritmo en escalones se manifiesta mui levemente o está abolido siendo, por tanto, mui grande la retención salina i la hidratación.

Este enfermo en que, por sus condiciones digestivas, es imposible la ingestión diaria de 10 grs. de sal por tres días, sin que se produzcan vómitos, se verificó la exploración como muestra la tabla adjunta. 8 grs. para el primer día, 18 grs. para el segundo (8 de alimentación i 10 por obleas) i 7 en el tercero. Como lo importante en este examen es observar el ritmo de retención i eliminación, i la cantidad retenida, poco importaba que el equilibrio se estableciese con 7 o 20 grs. siendo lo indispensable que este se verifique en el tercer día.

Al hacer el total de la sal eliminada desde el momento en que se suspendió la cloruración hasta llegar a la cifra de equilibrio clorurado, se nota una diferencia de 2 grs. mas o menos lo cual se explica por la fuerte sudoración del paciente en ese día, cosa que también se aprecia en los demás.

El examen de la tabla también muestra que en el séptimo día hai notable oliguria (500 c. c.) lo cual no modificó la eliminación de 6.72 grs. de sal con que se establecía el equilibrio clorurado, al tercero de la cloruroración, debido al perfecto estado renal que elevó la concentración salina a 13,45; hecho que tiene mucha importancia, ya que el riñón siempre busca excretar los desechos a baja concentración, especialmente con el cloruro de sodio que a concentración poco más alta, le es nocivo (19, o 20‰).

A pesar de haber alejado todas las causas de error, se repitió la determinación del coeficiente ureosecretorio; pero haciendo variar sus factores mediante la ingestión de 15 grs. de urea y con régimen clorurado que siguió a la prueba anterior. He aquí los resultados:

Constante ureica de Ambard

Fecha Enero 29 de 1919.

Nombre V. P. Edad 23 años. Peso 62. 4 Kilos. Temperatura 37°. c.

ORINA: Vejiga evacuada a la 1 hora 22 minutos 30 segundos.
Orina recogida a las 2 horas 57 minutos 30 segundos.
Duración de la prueba 1 hora 35 minutos.
Volumen obtenido durante la prueba 99 cc.
Volumen referido a 24 horas 1.500,6 cc. Cloruros 7,18
(c) Concentración de urea, por litro 25,21 grs. (en 24 horas
(d) Caudal de urea, referido a 24 horas, 37,83 grs.
Constante: K=0,07 normal.
SANGRE: (Ur) Cantidad de Urea por litro 0,489 grs.

$$\frac{Ur.}{\sqrt{D\times\frac{70}{P}\times}\;\sqrt{\frac{C}{25}}}=K;\quad \frac{0.489}{\sqrt{37{,}83\frac{70}{62{,}4}}\;\sqrt{\frac{25.21}{25}}}=K0.07$$

No hai albúmina.

El coeficiente permanece normal i las leyes de Ambard como siempre se han cumplido con exactitud:

La tensión arterial en este enfermo, marca:

Fechas	Máximas	Mínimas	Esfígmicas	Nº de Pulso
24 Dic.	13	8	5	98
27 ,,	13	8	5	90
6 Enero	13	7	5	84
13 ,,	13	7	6	88
20 ,,	14	8	6	80
28 ,,	14	8	6	76

Queda pues probado, que las funciones de eliminación urinaria están perfectamente intactas i además, que los síntomas mórbidos de este sujeto no se deben a alguno de los sindromes funcionales del Mal de Bright: Azotémico, Clorurémico-hidrópico, Hipertensión permanente, hallándose ausente también el sindrome urinario.

La alimentación variada, azoada, clorurada al gusto del enfermo, sin ningún perjuicio para él, son la prueba clínica más evidente de lo que el laboratorio nos afirmó.

La medicación oral seguida se redujo a leche de magnesia en las comidas i al mismo tiempo se le ponían enemas de agua i azúcar cada vez que fueron necesarios para combatir la constipación.

Hipodérmicamente pusimos diariamente una inyección de sulfato de estricnina a dosis progresiva llegando primero hasta la dosis de seis miligramos por inyección. Después de un reposo de cinco días comenzamos de nuevo i llegamos hasta nueve miligramos diarios. Posteriormente en otras series llegamos hasta doce miligramos diarios con perfecta tolerancia. Los resultados fueron excelentes i dos meses i medio más tarde el enfermo se sentía bien, había recuperado las fuerzas y los reflejos; dormía bien, respiraba bien i el pulso en ritmo, tensión i frecuencia era normal. El anasarca había desaparecido i su peso era de 134 libras. También se le hicieron a este enfermo, metódicamente, masajes eléctricos para prevenir la atrofia muscular.

Este caso es bien interesante para nosotros; pone de relieve lo fácil que es confundir la forma hidrópica del beriberi con una nefritis hidropígena, i nos ha permitido probar que las funciones renales se cumplían a satisfacción, que las crisis dispneicas, tampoco obedecían a un factor urémico.

Posteriormente hemos tenido ocasión de estudiar la función renal en otros seis casos de beri-beri, el uno de ellos en una señorita C. G. de 19 años de edad, natural de Guayaquil, en la cual también se había hecho el diagnóstico de nefritis hidropígena, la que estaba en suma gravedad: el pulso era de 140, había también accesos de dispnea, constipación rebelde, paraplegia, anestesia del dorso del pié, i en la cara externa del muslo; adormecimiento de las manos, anemia profunda, los esfinteres estaban normales, sensación de angustia i opresión mortales en la base del torax, insomnio, náuseas i anorexia. La enfermedad habíase iniciado 54 días antes i al comienzo hubo fiebre moderada i remitente que duró aproximadamente una semana, siendo apirética la evolución ulterior La enferma vive en los arrabales de la ciudad i es mui pobre. No hai antecedentes personales ni familiares de alcoholismo. La constante de Ambard dió el resultado siguiente:

$$\frac{0.187}{\sqrt{6.00\times\frac{70}{39.36}\times}\;\sqrt{\frac{12}{25}}}=\text{K: }0.066$$

Cloruremia	5.50	Umbral—5.451
Debit	0.50	Exceso —0.049
Concentración	1.00	
Albúmina 8 gr.	por litro.	

Como se vé el índice urémico es bastante bajo, la constante uréica normalísima, secreción clorurada normal i todo esto a pesar de la gran albuminuria, tampoco hai cilindruría. Por esta razón hemos seleccionado este caso, para hacer ver como no obstante dicha albuminuria ambas secreciones de urea i cloruros permanecían normales. En los otros cinco casos no existía albuminuria i las funciones renales también se conservaban íntegras, siendo todos ellos casos de la forma hidrópica.

No hemos aplicado el estudio de la permeabilidad renal al azul de metilo i a la fluoridzina por cuanto el estudio de la eliminación de las sustancias normales que hemos practicado nos parece el mejor medio de estudiar la función renal. Con los resultados obtenidos, podemos deducir que el edema en los beribéricos, no reconoce por causa una retención hidroclorurada.

No hallándose dilucidada la etiología del beriberi, resulta bastante difícil i hasta hipotético el emitir teorías para explicar la fisiopatología de sus síntomas. Podemos sinembargo hacer congeturas por exclusión, que si no nos permiten afirmar con exactitud que tal o cual síntoma se debe a tal o cual causa, podamos afirmar con toda certeza que no se debe a tales o cuales otras.

Tratándose de los edemas por ejemplo, en vista de los resultados obtenidos de nuestras observaciones que dejamos ya expuestas, dedujimos que en ellos no influye para nada la insuficiencia renal, ya que, como lo hemos demostrado, el riñón conserva su integridad funcional; lo cual constituye un dato importantísimo que en caso necesario puede ser de gran ayuda para el diagnóstico, ya que es fácil en ciertos casos confundir las dos enfermedades, especialmente cuando se trata de la forma hidrópica del beri-beri.

La falta de resistencia de la pared de los vasos se ha aducido como causa de los edemas en el beri-beri, por parálisis vasomotora, teoría bien sugestiva al primer momento, de cuyo lado dejamos de inclinarnos, exclusivamente, si tomamos en cuenta que los edemas se producen rápidamente, antes de que exista parálisis i antes de que las lesiones de los nervios sean apreciables. Se han presentado: la hipótesis de que la vaso dilatación fuese producida por la presencia de sustancias tóxicas en la sangre i la teoría de la alteración de las paredes vasculares por dichas sustancias. Respecto de estas dos teorías diremos que hasta hoi nadie ha comprobado histo-patológicamente la lesión de la paredes capilares i mientras esto no se verifique, permanecerá esta teoría tan sólo en el terreno de las hipótesis. Respecto a la anterior, mientras no se demuestre la existencia de las toxinas circulantes, tampoco tiene esta teoría mejores condiciones de comprobación. Todos sabemos, que después de los trabajos de Funk, se tiende a reconocer como causa de esta enfermedad la falta de vitaminas, haciéndola, la primera en este nuevo grupo de las avitaminosis, no sería pues presencia de sustancias tóxicas sinó defecto de sustancias útiles la causa de los diversos síntomas de la enfermedad. Debemos por otra parte recordar que antes del descubrimiento de la retención hidroclorurada en el mal de Bright eran estas teorías mismas de la vasodilatación i de la alteración de las paredes vasculares por la presencia de sustancias tóxicas en la circulación sanguínea, las que contaban con la gran mayoría de adeptos i ya conocemos como el importantísimo descubrimiento de Widal desvaneció todas estas hipótesis. En medicina como bien lo dijo Charcot, los hechos son lo primero, las teorías deben venir después i cuando no se procede de acuerdo con tal axioma, estamos expuestos a ver nuestras teorías derruirse como un castillo de naipes.

Con la boga de las glándulas de secreción interna debía venir una explicación fundada en un trastorno funcional por exceso o por defecto secretorio de alguna de ellas i en efecto se ha dicho que la avitaminosis beribérica produce un hiperfuncionamiento de las suprarrenales, con la consecutiva hipertrofia i la consiguiente producción exagerada de adrenalina (Vaquez, Josué) i la resultante hipertensión capilar i la producción inmediata de los edemas. Esta teoría como las anteriores padece de la falta de hechos que le sirvan de apoyo: no hemos encontrado señalada la hipertrofia suprarrenal i el estudio de la presión arterial en todas nuestras observaciones demuestra que en vez de hallarse alta, está normal o baja.

Si en el beri-beri el edema estuviera limitado a los miembros inferiores, cabría pensar o discutir en cirrorosis hepática, en obstrucción de la vena cava, en flebitis, en compresión de los vasos linfáticos, pero como el edema llega al anasarca, ninguno de estos factores cabe ser discutido en el beri-beri.

Tampoco cabe pensar en edema por insuficiencia tiroidea, por cuanto entonces el edema tiroideo es mucho más duro i va acompañado de un complejo sindrómico mui diverso.

Nos queda considerar la hipótesis del origen cardiaco de los edemas.

El edema beri-bérico comienza por los miembros inferiores i todos los patólogos están conformes en que la gran mayoría de los edemas que comienzan por las estremidades inferiores reconoce un orígen cardiópata. Cabot precisa números en su estadística: 8,236 cardiacos sobre 4,987 de otras enfermedades. (Differential Diagnosis Vol. II pag. 467).

Sir Patrick Manson (Tropical Disease pag. 417) llama la atención sobre los súbitos ataques cardiacos que terminan rápidamente por paresia i sobre distensión del corazón con edemas pulmonar, hidropericárdico e hidrotorax, i más adelante, (pag. 424). la debilidad cardiaca i la parcial supresión de la orina pueden ser causa de los edemas i al tratar de la anatomía patológica encuentra que el corazón está dilatado, especialmente el derecho, con gran acúmulo de sangre en su interior, lo mismo que en las venas.

P. Scheube reconoce que el corazón necesita ser especialmente atendido i que el digital es una droga *indispensable* en el beri-beri, (Diseases of warm countries pag. 211)

Deschamps (Beri-beri vol VI Traité de Med Brouardel-Gilbert) encuentra en las autopsias el corazón engrosado, flácido i el derecho dilatado, lleno de coágulos amarillentos, resistentes, que se propagan en la arteria pulmonar i el miocardio atacado de degeneración gránulo-grasosa.

Hebrard (Traité de Path Exot de Grall i Clarac vol. V pag. 19) dice: el corazón nadando en un abundante derrame pericárdico, comprimido en la masa líquida, dificultado en sus movimientos i atacado en su tonicidad lucha penosamente i acelera sus movimientos para vencer la dificultad general de la circulación. Si este estado se prolonga la fibra cardiaca no llega a vencer todos estos obstáculos, se distiende, las cavidades se agrandan, una hipertrofia pasiva por debilidad del miocardio, se produce i se complica a menudo de insuficiencia valvular. La fibra cardiaca sufre en su vitalidad i su degeneración se produce. La muerte sobreviene por detención del corazón, ya en síncope brusco, ya por debilidad progresiva.

Sacquepée (pag. 74 vol. VII du Traité de Medecine Widal, Roger, Teissier) dice: el corazón está siempre profundamente tocado, especialmente el derecho, la aurícula i el orificio tricúspide están dilatados, la degeneración grasosa parece ser la más habitual, pero no se han constatado formaciones embrionarias, de tal manera que la lesión cardiaca debe ser considerada como degenerativa i es sin duda consecutiva a las alteraciones del pneumogástrico, del plexo cardiaco i de las terminaciones nerviosas intracardiacas constatadas por Jeanselme i Aoyagi.

Scilling (Tratado de Med. Int de Mohr i Staehlin pag. 582 vol. II) dice: el edema subcutáneo es causado por la acción cardiaca disminuida. A la autopsia señala también la dilatación del corazón derecho, el color pardo oscuro del miocardio, i en las lesiones microscópicas dice: la musculatura del corazón reacciona de modo especial al veneno beribérico. No sobreviene multiplicación de los núcleos, sino que la sustancia contractil desaparece, de modo que quedan fibras como tubos en las cuales la estriación trasversal ha sido sustituida por una granulación. Además sobrevienen también focos de infiltración, que más tarde se convierten en zonas membranosas esclerosadas.

Castellani i Chalmers (Manual of trop. med. pag. 1682) dicen: el corazón derecho está siempre mui dilatado en los casos agudos; el miocardio presenta degeneración grasosa con segmentación i vacuolación de las fibras e incrementación del tegido intersticial. Estas alteraciones son idénticas a las encontradas en los curieles a la sección del pneumogástrico.

Jeanselme i Rist (Precis de Path Exot pag. 389) a más de señalar la dilatación del corazón especialmente del derecho i la hipertrofia de sus paredes en los casos crónicos, i la alteración macroscópica del color del miocardio i la presencia de cuágulos en las cavidades, dicen: la degeneración de la fibra cardica ofrece varios grados i está desigualmente repartida, predomina en la pared del ventrículo derecho i en los músculos papilares que a menudo se encuentran señalados por manchas i estrias amarillentas. En los cortes de miocardio que hemos examinado, al lado de fibras de estructura normal, se veían otras vacuoladas conteniendo grasa. La estriación transversal era netamente visible. No encontramos nódulos infecciosos, ni infiltraciones embrionarias, ni degeneración de los vasos, en una palabra no hemos encontrado ningún indicio de proceso inflamatorio: las lesiones eran puramente degenerativas.

D. B. Simmonds, sobre miocardios de coloración amarilla, encontró alteraciones histológicas tan considerables que le fué difícil hallar una sola fibra que hubiese conservado su estructura normal, todos los elementos habían perdido sus estrias transversales i sufrido la degeneración granulosa.

A le Dantec (Maladies des pays chauds pag. 615) repite la misma cosa respecto a la degeneración gránulograsosa, la dilatación de las cavidades i el cambio de coloración.

Sir W. Osler [Tratado de Pat Int ed española pag 615] dice: las fibras del miocardio presentan una degeneración mui pronunciada.

Duerck [Verhandlungen d. deutch pat gessellchaft Sep 1918] en un caso en que el miocardio estaba blando i dilatado, observó que las células musculares parecían dislocadas, infiltradas por una masa vitrosa homogénea dispuesta en forma de bandas o manchas que se continuaban insensiblemente con el protoplasma estriado de las fibras cardiacas; quedóse admirado de la rapidez con la cual se produjeron semejantes lesiones.

Dopter, Rathery i Ribierre (Traité de Path Int pag 479) dicen: el corazón está dilatado i flácido; se nota al microscopio la degeneración gránulo-grasosa del miocardio.

I así de los demás: las alteraciones del miocardio que se traducen macroscópicamente por la vacuolación de sus fibras i por la degeneración gránulograsosa i la pérdida de las estriaciones transversales, es un hecho incontrovertible en el beriberi; que tales lesiones son causa de la muerte en estos casos, no cabe duda.

La falta de buen funcionamiento del miocardio apareja edemas, es también indudable, i constituyen uno de los signos precursores de la disistolia, luego no es ni puede ser más fundada la teoría de que la disistolia es uno de los factores más importantes en la producción de los edemás del beriberi i al respecto podemos pues afirmar que el corazón es en gran parte culpable de la producción de los edemas con la misma seguridad que hemos tenido para declarar inocente al riñón.

Otro factor que no es indiferente en la producción de los edemas es la probable intervención de los tegidos.

A. Meyer i G. Schaeffer han demostrado que el poder de inhibición de un tegido está en relación con su tenor en lipoides i es tanto más elevada cuanto mayor sea la relación $\frac{\text{colesterina}}{\text{acidos grasos}}$ denominado coeficiente lipocítico.

Achard, Ribot i Leblanc han encontrado que en el hombre el coeficiete lipocítico, en estado fisiológico, conserva un valor uniforme que oscila dentro de 0,35 i 0.40. Así también los mismos autores demostraron que en los brighticos edematosos dicho coeficiente es siempre superior a 0.50‰.

Después de los trabajos de Widal no han faltado investigaciones tendentes a probar que el edema está ligado a una intoxicación por productos orgánicos. Timofeew inyecta el suero de animales nefrectomisados, suero que es tóxico, pero que no produce edemas. El suero de los nefríticos contiene según él dos órdenes de sustancias, tóxicas unas, linfagogas las otras i dá a estas el nombre de nefroblaptinas. Concluye, que los edemas son debidos a la acumulación de sustancias orgánicas elaboradas por el riñón en ciertas nefritis: la retención clorurada sería secundaria; las cristaloides i el agua irían a fijarse sobre los coloides que representarían la verdadera causa de las hidropesías.

A primera vista según esta hipótesis, podría pensarse que los edemas constituyen una vasta compuerta para las sustancias tóxicas que irían a depositarse en un tejido poco importante. La experiencia hecha por Baylac i Boy Tessier arruina tan seductora hipótesis ya que según aquella 273 cc. de líquido de edema inyectado a conejos no es más tóxico que el agua salada. En tratándose de las nefritis hidropígenas es pues la retención hidroclorurada de Widal la que domina hoi en la ciencia.

Tratándose del beriberi en el cual hemos demostrado, la integridad del funcionamiento renal, los edemas podrían acaso tener por causa la presencia de sustancias linfagogas como pensó Timofeew en las nefritis. Sería pués interesante estudiar la toxicidad del líquido del edema beribérico, i mientras no se realicen experiencias en tal sentido, nada se puede concluir al respecto.

Respecto a la existencia de otros factores de origen vasomotor o vasonutricio es mui probable su existencia, pero mientras no sean comprobados con hechos, lesiones anatomo patológicas i estudios experimentales, no podemos salir respecto de ellos del terreno de la hipótesis.

I no podrán ser resueltos definitivamente todos estos problemas mientras nuestros conocimientos sobre la naturaleza exacta del beriberi o kaké no sean más seguros i claros.

CONCLUSIONES

1ª.—El Beriberi existe en determinadas zonas en la República del Ecuador.

2ª.—Las funciones renales se conservan indemnes en el beriberi–tanto la secreción ureica como la clorurada.

3ª.—Los edemas en esta enfermedad son independientes de toda retención clorurada.

4ª.—Las alteraciones estructurales anatomapatológicas de la fibra cardiaca i sus trastornos funcionales son uno de los factores hidropígenos más importantes en el **Beriberi**.

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THE EPIDEMIC DISEASE

[Beri-Beri]

IN THE

RICHMOND DISTRICT ASYLUM, DUBLIN.

REPORT TO HIS EXCELLENCY THE MINISTER OF MARINE,
By DR. A. F. VERSCHUUR, Dirig. Off. v. Gez.;
And DR. G. VAN IJSSELSTEYN, Off. v. Gez. 1e. kl.

TRANSLATED BY
DANIEL F. RAMBAUT, M.D.;
Assistant Physician and Pathologist, Richmond Asylum, Dublin.

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RICHMOND DISTRICT ASYLUM IN DUBLIN

TRANSLATOR'S PREFACE.

In the summer of 1894, a strange epidemic broke out in the Richmond Lunatic Asylum (see the published writings of Dr. Conolly Norman on the subject). A second epidemic began about the middle of August, 1896, and a third early in July, 1897.

At the invitation of Dr. C. Norman, Rear-Admiral Hodenpyl, Inspector of the Marine Medical Service, sent a commission, consisting of Dr. A. F. Verschuur and Dr. van Ijsselsteyn, to Dublin, to investigate the cause or causes of the epidemic, and, if possible, to determine the conditions that favoured its propagation. Their stay lasted from the 16th to the 21st of August, 1897. On their return to Holland they issued a joint report, of which the following is a translation.

Consistent with clearness, I have tried to be as literal as possible; but, to render the meaning the more distinct, I have, here and there, inserted an unimportant word or phrase for which no equivalent exists in the original. Such words or phrases it has seemed to me advisable to place within brackets.

D. R.

TRANSLATION.

In 1814, the Richmond District Asylum was founded for the treatment of the insane of the whole of Ireland. Since 1831 it has, however, been set apart, exclusively, for the counties of Dublin, Louth, and Wicklow, and also for the Cities of Dublin and Drogheda.

At first the institution consisted of a stone building capable of accommodating 240 patients. Since 1833, the place has been more and more extended, in order to meet the ever-increasing number of those for whom admission was requested. On account of the overcrowding of the institution several wooden buildings were erected in 1893, 1894, and 1895, as a temporary provision.

At present the Asylum contains over 1,700 patients, together with 200 nurses, male and female. The area of its grounds is 54 acres. They are situated on the north side of the city, at an altitude of from 20–30 metres above the level of the sea, and are bounded by the female prison, the workhouse, with about 3,000 inmates, and the House of Industry Hospitals, holding about 200 beds. The grounds are also surrounded by private residences and labourers' cottages.

The various stone and wooden buildings look very clean, and are partly painted, partly whitewashed. Never has arsenic or other substances injurious to health formed an ingredient of the paint. The ventilation is fairly good: our observations were made in the summer, when doors and windows could be opened without producing any troublesome draught. The buildings are warmed by means of hot-water pipes.

In rainy weather the ground-floor rooms of some of the stone and wooden buildings seem damp, by reason of being situated too low. The wooden floors, also, leave something to be desired. Lately, those in charge have begun to wax the wooden floors and fill up the chinks in order to exclude the damp. It is only in a few large rooms this has not yet been done, the floors being cleaned with water in the old way.

For sleeping accommodation, there are in use iron bedsteads with wire woven mattresses that are filled with hair. The bedclothes leave nothing to be desired. As regards the personal clothes of the patients confined to bed, they appeared to us to be rather light. Indeed, they are sufficient for persons who will remain quietly under the sheets, but not so for restless patients inclined to toss about or to jump out of bed.

In many of the dormitories the beds were placed too close to one another, and this was especially the case in the Female Department. Corridors and passages are, here and there, used for sleeping purposes; so that, in proportion to the space, by far more patients are lodged than can be justified on hygienic grounds. During the day, however, the greater part of the patients spend their time in the gardens and dayrooms.

The stone floors of the kitchens, and of a few of the bath-rooms in the men's department, leave much to be desired; for grease and dirty water can easily accumulate in the wide fissures between the flags, thereby providing an excellent medium for the development of micro-organisms.

Since 1887, excreta are removed by means of a new sewerage system falling into the Liffey, a river which flows through the City of Dublin. Prior to 1887, the drainage was very bad, and the soil must have been infected with sewerage. It was to this the many cases of dysentery, which formerly occurred in the institution, were chiefly attributed. After 1887 the number of patients suffering from this disease decreased considerably. However, during the last few years several cases have again occurred; and for these the Medical Superintendent of the Asylum, Dr. Conolly Norman, could not assign a cause. The present drainage is eminently satisfactory, and the drinking water is of a very good quality, as has appeared from repeated chemical examinations. Dr. Norman considers it impossible that the milk supply could have been the vehicle of the infections germs, for the contractor supplies the same quality of milk to other institutions where dysentery has not occurred.

The water supply of the Richmond Asylum is from the same source as the water supply of the city; that is to say, a mountain stream in the Co. Wicklow. There the water is filtered and thence conveyed through iron tubes to the city, where, before it is used, it is again filtered. In the Asylum the water is carried through the various buildings and apartments in tubes such as are used in Holland. Factories which could possibly contaminate the water, are not to be found in the vicinity of the water source.

A few litres of water which had remained over-night in the tubes, were taken away by us to Holland, where it was examined by the Chemist of the Royal Dutch Marine, Dr. Simon Thomas, who declared it to be excellent drinking water.

The different articles of food for the use of the institution are purchased in the city from contractors, who, also, supply the workhouse and other institutions. In none of the latter [all of which are] in the immediate vicinity of the Asylum, have cases occurred of the peculiar disease treated of in this report. The store-rooms for the provisions that we visited gave no ground for criticism; and so far as could be ascertained the quality of the bread, butter, sugar, tea, fresh meat, and vegetables was very good.

Rice (peeled) is given only in small quantities—373 stones per annum; that is to say, about 2,400 kilos. It is consumed chiefly by epileptics in their soup. A far greater quantity of potatoes boiled in their skins in accordance with the Irish custom, is supplied.

Mainly, the food is cooked by steam. The kettles and other utensils are made of iron or tin. We saw only a few kettles made of copper; but these were well tinned on the inside. A dinner at which we were present gave the impression that, both in quantity and quality, the patients' food was excellent. Different classes of patients are not under different systems of dietary, and sufficient care has been taken to ensure variety in food.

The disinfecting apparatus (Washington Lyons' Patent) consists of an oven and boiler placed in a detached stone building, divided by a stone wall into two compartments. In one is the boiler and the greater part of the oven; in the other, the remaining part of the oven. Articles about to be disinfected are brought in at one side and placed in the oven, and after being sufficiently disinfected are removed from the other side. Disinfection takes place according to the nature of the articles, by either hot air, or steam, or both. As the highest temperature attainable is 135° C., it is, consequently, fully sufficient for disinfecting purposes. It is customary to disinfect all articles of new patients. When mattresses are disinfected the contents are entirely taken out; the hair is disinfected in the oven, and the covers are burned.

The laundry is a building made up of several divisions. In the first, the clothes are boiled in large boilers. In the second, they are washed clean with soap. In the third, they are dried in the drying apparatus, and in the remaining divisions they are prepared for renewed use. Finally, they are removed by a separate exit.

This Asylum was, during the summer and autumn of 1894, attacked by an epidemic, the chief characteristic of which seemed to be an inflammation of the peripheral nerves. Not unfrequently the attack began with vomiting and diarrhœa, sometimes with vomiting alone, and during the first day, or first two days, the temperature was slightly raised. In very many cases, however, these appearances were not noted; while complaints were made of lassitude, palpitations, dyspnœa, and heaviness of the legs, accompanied by shooting pains, especially at night. On investigation œdema was found to exist. It was most distinctly visible on the lower parts of the legs, on the tibia and ankles. Over the tibia the soft parts were very sensitive. There were anæsthetic spots, most constant on the lower part of the legs. Frequently the edges of such spots were markedly hyperæsthetic and sharply defined. The œdema sometimes greatly increased, and was not merely confined to the lower parts of the legs, but became general. It spread over the sacrum and sternum; also the face, which was more or less swollen and assumed a peculiar expression. This œdema could not be ascribed to disease of the kidneys, because albumen was not once discovered in the urine.

The muscles of the lower limbs, especially the calves, were, in the beginning of the disease, hard to the touch, and on pressure very painful. Subsequently they atrophied, often in a high degree. Also the muscles of the upper extremities were not unfrequently attacked.

The changes in the heart were generally confined to enlargements towards the right. Occasionally, there was accentuation of the second sound [the second heard in the pulmonary area]; but in other respects nothing existed to indicate a lesion of the valves. The action of the heart was in all cases frequent and weak; and its frequency was greatly increased by the slightest exertion—for instance, by an effort to get out of bed. Often it was irregular, sometimes intermittent. In a number of cases, after a few pulsations of about equal force a weaker stroke followed.

The disappearance of the œdema did not always take place slowly: on the contrary, sometimes very rapidly, in a few days, or within twenty-four hours. Not till then did the atrophy of the muscles become clearly visible, most commonly on the lower, but sometimes also on the upper extremities. The muscles were thin and relaxed. The skin covering them was moderately œdematous, showing, occasionally, a slight pigmentation not ascribable to a previous lesion.

At this stage the knee reflexes, which at the beginning of the disease were generally raised, had invariably disappeared.

So relaxed had the joints become, that if the patient lay on his belly the heel could easily be pressed against the gluteal region.

Dropped feet, accompanied by claw-like deformity, the result of paralytic contractions, occurred as a consequence of paresis or paralysis. Standing alone was, in some cases, just possible; but on the slightest deviation from the perpendicular position the patient fell. Some could move forward only in a sitting attitude, and with the assistance of their hands. The paresis of the muscles of the arm, never so pronounced as that of the lower extremities, and far less frequently in evidence, caused dropped wrists.

Sometimes a fatal issue followed in consequence of paralysis of the heart and œdema of the lungs, conditions which were generally associated with hydrops pericardii and hydrops pleuræ. But, in the great majority of cases, the disease did not take such an alarming course. In most cases the symptoms were limited to complaints of lassitude, pains in the legs, general feeling of debility, palpitations, and dyspnœa on going up stairs. Enlargement of the right side of the heart was discovered; also œdema, especially of the lower part of the legs. Frequently anæsthetic areas existed on the lower parts of the legs, back, breast, &c., and were generally accompanied by hyperæsthetic zones. These anæsthetic and hyperæsthetic spots were inconstant: some were observed which remained visible only for a day, others even not longer than an hour. Hyperæsthesia over the crista tibiæ, on being touched [in that region], was a very constant symptom. If the patient remained in bed and received good food these slighter forms got generally cured within a few months. Treatment with the continuous current seemed to exert a beneficial influence on the slightly atrophic muscles.

As to the diagnosis of the disease just briefly described, and which may be regarded as having occurred in an epidemic form, for it attacked 127 male and 47 female patients (of whom 18 male and 7 female sufferers died), Dr. Conolly Norman, the Superintendent of the Asylum, was induced to believe it was beri-beri. In this diagnosis he was supported by the opinion of other specialists in tropical diseases (Dr. Walter Smith and Sir T. Stoker); also, by the unreserved decision given on the spot, after careful investigation, by Dr. Patrick Manson. Dr. Manson, who at one time practised in China, now lives in England, and is recognised as a specialist in tropical diseases in general, and, in particular, on beri-beri, a disease on which he has written a valuable monograph. The epidemic began in June, 1894—at least it was then for the first time as such recognised. Dr. Norman, however, directed our attention to the fact, that it was quite possible cases might have occurred prior to that date; and this seems highly probable if one takes into consideration the great number of deaths from paralysis of the heart which immediately preceded the epidemic. Possibly, in many cases, the paralysis of the heart was only a symptom of the as yet unrecognised beri-beri. The epidemic increased in violence until October, and then rapidly decreased; so that after the first half of that month no new cases presented themselves. So much for the epidemic of 1894.

The cause or causes of the disease were sought after with the greatest zeal, and every effort was made to discover the conditions that favoured its propagation. Neither in the water, which was repeatedly examined, nor in the food, which might be described as very good, could anything suspicious be found. Moreover, the water was exactly of the same kind as that which is drunk by the whole City of Dublin. Again, the food was not different from that consumed by a number of private individuals and in public institutions, and yet no similar disease presented itself elsewhere. Already, in the beginning of this report, we treated of this subject in full detail. [Then], assuming that the disease was beri-beri, nothing else was left but to pre-suppose the causes to which in tropical countries beri-beri is generally referred—such as over-population, insufficient ventilation, infected or damp soil, infected wood work (to this last factor especially Dr. Patrick Manson attached great importance).

In the middle of August, 1896, again, an epidemic broke out, which increased during the autumn and beginning of winter, reaching its maximum in the early days of December, when, altogether, there were then 113 patients suffering from the disease. Soon it rapidly decreased, though a few isolated cases occurred during the months of January, February, and March, 1897, and even up to the summer. The number of deaths amounted to 7 male and 2 female sufferers. And, whereas in the former epidemic, doctors and attendants had remained free, in the second epidemic 7 female nurses were attacked.

In this epidemic also, *post-mortem* examination revealed degeneration of the heart muscle, œdema of the lungs, hydrops pericardii et pleuræ and anasarca.

The third epidemic may be considered as having begun on June 1st, 1897. On that date, there were still 4 male and 6 female patients suffering from the symptoms of the last epidemic. On June 3rd a patient was attacked who had suffered from this disease in 1894. From that date until the end of June, 9 female patients were attacked. In the month of July, 81 female patients and three nurses, and 30 males, amongst them one attendant, were attacked; so that within two months the total number of patients amounted to 124.

Now, although the epidemic appeared the most serious as regards numbers, yet in form it was mild, most cases being of a rudimentary type. One female patient died. Many of the patients (27 female and 11 male, together with one female attendant) had had a previous attack.

Such was the state of affairs at the end of July, 1897, when the Rear-Admiral, L. P. Gysberti Hodenpyl, Inspector of the Marine Medical Service, who takes a special interest in these epidemics, entered into a correspondence with Dr. Conolly Norman, Superintendent of the Richmond District Lunatic Asylum, with the result that we were sent to Dublin to investigate the causes and symptoms of this epidemic, and, if possible, to ascertain if the disease was identical with the beri-beri which occurs so frequently in our colonies.

In order to give a clearer insight into the question, we have already spoken of the diet and general state of the Institution: we have also given a succinct review of the principal symptoms and the course of the disease in the three epidemics. At the time of our visit to the Asylum, from the 16th to the 21st of August, there were suffering, of the patients, 42 males and 143 females, and of the attendants 2 males and 4 females. It is by no means an easy matter, within the brief period of a few days, to acquire a correct idea of the nature of an epidemic such as is here spoken of. To us it seemed best to study accurately a few cases which may be regarded as types of the three epidemics, and, in addition, to examine as many patients as possible, with a view to discover to what extent their symptoms differed from these types. The remainder of our time we profitably employed in investigating whether the most striking features of beri-beri, as it appears in our colonies, were also prominent symptoms in the disease which appeared in the Asylum.

It will not be thought out of place to here return a word of thanks to the Superintendent, Dr. Conolly Norman, for his great kindness and clear information; also to his medical staff, especially to Dr. Rambaut, who showed such readiness to afford us every assistance.

Of some of the most typical cases we give short histories. These records are from detailed notes made by the attendant physicians. The latter have also, at our request, made notes of some other cases that greatly interested us. From these histories we have been able to form an idea of the manner in which the disease manifested itself in the three different periods.

In the first epidemic the symptoms were most serious, in the third it spread by far more rapidly, but the patients were less dangerously attacked. In all other respects there was no difference, except one of degree, between the three epidemics. It is a remarkable fact that those who had been already attacked ran a great risk of a second attack.

In the preceding brief description of the symptoms of the disease, we have emphasised the circumstance, that a considerable number of the cases began with vomiting and diarrhœa, or with vomiting alone, and a slight rise of temperature. Our attention was attracted to this circumstance while we were studying the typical cases already referred to. We are aware that in cases of intoxication proceeding from the intestinal canal with rise of temperature, violent pains are felt in the calves, while the muscles of these parts are as hard as a plank and painful on pressure. In the investigation of the ætiology of the disease this symptom appeared to us of the greatest importance. Dr. Norman and his staff assured us that this symptom was very frequent, but that it did not occur constantly is certain.

Generally, those attacked came under treatment after having complained of lassitude, pains in the legs, oppression of the chest, and certain subjective symptoms. The latter were:—Sensation of walking as if on felt, feeling as if ants were creeping over the body, painful formication (the pirri-pirri of the Japanese beri-beri), pricking of pins and needles, anæsthesia dolorosa, shooting pains through the calves (described by the patients as though they were caused by the blow of a whip), burning pains, and cold and hot shiverings without fever. These symptoms require no further explanation.

In the great majority of the cases, by reason of the circumstance of the patients being insane, it was not possible for us to obtain satisfactory information. The clearest and most detailed histories are those of the male and female attendants affected. The anæsthesia and hyperæsthesia were of a very variable nature as may be inferred from the following histories of cases:—

Th. M. O. (male attendant), entered the Asylum on January 11th, 1897. Was always in good health, and discharged his duties with intelligence. On August 2nd, he had a slight fever which lasted for two days, also a feeling of numbness and tingling in the left leg. Occasionally, both legs were "asleep," with a feeling of pricking of pins. Œdema over the tibiæ, more marked over the left than the right. On the left, the œdema extends from the knee to the ankles, but not on the dorsum of the foot. The skin, especially that over the lower half of the calf of the leg, felt thick. No anæsthesia. Pulse, 124, when at rest; but it reaches 140 after movement of the arms. Pulse regular, weak, not intermittent, but, now and again, one stroke was weaker than the preceding ones. Heart sounds pure. Urine acid, free from albumen. At night the patient was much troubled with pain in the calf of the right leg.

August 3rd. A feeling of heat on the inner side of the lower part of the left leg. Pulse 80, and regular. Appetite good. Discharges regular. Prætibial œdema. No anæsthesia.

August 4th. He felt a little better in the morning. He soon becomes tired after walking. A feeling of numbness of the legs as though they were asleep, accompanied by a sensation as if caused by pricking of pins and needles. He feels no pain on pressure of the lower parts of the leg; but, subsequently, a feeling as of pricking of pins and needles (retarded sensation) is experienced in those parts. Pulse markedly increased in frequency after the slightest exertion.

August 5th. The heart, now and then, intermittent; sometimes a feebler beat; stinging pains in the soles of the feet, and a pricking sensation in the toes.

August 7th. Pains in both forearms; pains over the tibiæ and over both inner surfaces of ankles. Sense of touch normal.

August 8th. During the whole night he felt pain on the inner surface of the left leg; two or three times he felt violent pains along the left arm, but they rapidly disappeared; still feels burning pains on the inner surface of the left tibia.

August 9th. In both legs there is a feeling of pricking with pins and needles, and a slight feeling of numbness along the inner surface of the right leg. Sense of touch normal.

August 11th. Pains in both legs from knees to feet, accompanied by a feeling of heat and stinging. Hyperæsthesia in the same regions and pains in the muscles on pressure.

August 19th. The patient declares he now feels no pain; but, that if he stands for a quarter of an hour his legs become very hot, and that he feels tired. Then the soles of his feet begin to tingle, and he has a feeling of formication; he feels the ground under him very well as he moves. No heart murmurs. Pulse 120, increasing to 155 during examination, by which apparently he was excited. Well marked *tache meningitique.* Pharyngeal reflex could not be excited. Galvanic excitability over the m.m. peronei and tibiales antici normal. Syphilis, it would appear, can be excluded.

R. O'B. (a female nurse), was always strong and enjoyed good health.

July 1st, 1897. Diarrhœa and vomiting.

July 2nd, 1897. In the same condition as day before. In the evening, as she attempted to assume the sitting posture, she had an attack of syncope; pulse very frequent; slight prætibial œdema; no albumen in urine.

From July 2nd to 13th, œdema variable, disappearing and reappearing; no disturbances of sensibility.

July 13th. Anæsthesia extending downwards from the popliteal region; a feeling of numbness in left calf, and pain in both legs.

July 14th. An anæsthetic zone from knee to calf on the left side; a smaller anæsthetic spot on the upper part of the calf of the right leg. Heart's action regular; second sound heard in pulmonary area accentuated; pains in the knees and around the ankles; no anæsthesia of the face.

July 15th. Anæsthesia over the whole thighs and legs, and, in addition, tender spots, especially over the lower part of the tibia. Great pain in thighs and knees, and cramps in the calves. Hyperæsthesia over sacrum (perhaps attributable to constantly lying in bed). A feeling of pricking of needles in the legs. Anæsthesia in the lumbo-gluteal region.

July 17th. Dropped feet; anæsthesia of thighs and lower parts of legs; both forearms are œdematous; the pulse is small and of variable volume: its frequency increases on slight exertion; the heart sounds are pure and regular.

July 30th. Sensation in the supra-mammillary region has altogether disappeared. After three days it returned and great hyperæsthesia and pain in that place.

July 31st—August 3rd. Neuritic pains of a violent nature in the back of the neck, and formications over the painful spots. Burning pains all over the back (painful formications, the pirri-pirri of the Japanese beri-beri).

August 3rd–5th. All feeling on the left side of the back has gone; still dropped feet.

August 5th. Feeling on left side of back has returned.

August 10th. All pains are gone and sensation is fully restored. There exists only hyperæsthesia over the inferior third of tibia, together with slight œdema. Pulse, 70, with body at rest; rises to 100 on moderate exercise.

August 19th. On our examination patient seemed to have fairly recovered; there were no cardiac irregularities, save that the pulse rose considerably after any movement.

Excitability of the m.m. tibiales antici and peronei were found to be normal. There existed in this patient a moderate degree of anæmia, which, according to the unanimous opinion of the attendant physicians, could not have developed until recently. An investigation as to hysteria yielded negative results.

The œdemas generally began on the legs over tibiæ and ankles. Frequently the dorsum of the foot remained free, the outline of the swelling forming above it a kind of manchette. Some œdema, even in slight cases, could be pointed out over the sacrum and sternum. If the œdema increased, then, general dropsy supervened—hydrops facialis, scroti, præputii, &c. This hydrops facialis can be easily recognised in the photograph of Th. G. The œdema at times almost entirely disappeared, but again returned with renewed severity. On the disappearance of the œdema, the atrophy of the muscles became more manifest. It is certainly a remarkable fact that the disappearance of the œdema occurred in some cases, within so brief a period as twenty-four hours. Most frequently the atrophy occurred in the muscles of the lower extremities, particularly in the lower part of the legs. How far it advanced, and what functional disturbances it produced may be imagined from the photograph of Th. G.

Th. G. entered Asylum, in 1884, with acute mania, which passed gradually into dementia. He did, and does still, some work on the farm. He was, until August 10th, 1894, in good bodily health and very vigorous.

August 10th, 1894. Œdema (general); no albumen in urine: heart sounds normal; pulse, 90 per minute when at rest. Further, no symptoms dependent on his mental state can be discovered.

August 25th, 1894. The œdema had gradually disappeared; but it is returning now more markedly, especially over the ankles and the tibiæ. Urine sp. gr. 1030; no albumen; no sugar. The patient is accustomed to sit on the floor by the side of his bed, supporting himself on his hand in the manner indicated in the first photograph.

August 26th, 1894. Pain on pressure of the shins, and on pressure of the muscles of the calves. The face is greatly swollen, especially under the eyelids (see photograph). He cannot stand unaided. Suffers from constipation.

August 29th. Very marked œdema of the legs; he cannot stand.

September 9th. Œdema has wholly disappeared. The atrophic form of the disease is now most marked. Knee reflex has disappeared. The feet are dropped and inverted.

October 20th. The condition, speaking generally, is unchanged. Plantar reflex increased.

October 27th. Patient can stand. From this date he improved and can again perform some slight work.

August 19th, 1897. To-day we find the man recovered from the disease as above described, which he went through in 1894. No irregularities of heart; pulse, 80; knee reflexes weak but clearly observable. The gait is not abnormal, and the muscles are not atrophied.

Not unfrequently, the patient becomes for life, an unfortunate cripple. Dropped feet generally appeared at an early stage. To what extent pressure of the bedclothes may have contributed to this result, for the patients lay constantly in bed, we shall leave undecided. Owing to the fact that some muscles had been affected less severely than others, paralytic contractures must necessarily have arisen. In a few cases the big toe had sunk below the level of the other toes, so that the second toe seemed to be riding on it (marked atrophy of extensor hallucis longus). The muscles of the upper extremity at times also suffered considerably. Many cases, indeed, were not very strongly pronounced; but yet clear instances of dropped wrist came under our notice. In the atrophy of the arms all the muscles shared in the trouble. Nothing appeared to us to indicate that certain muscles—for instance, those supplied by the radial nerve—were peculiarly liable to be attacked, or that other muscles, the supinator longus for instance, enjoyed any special exemption.

Whether the gluteal regions were involved was difficult to decide, owing to the mild course of the last epidemic and the trouble one had in examining the patients. We should be inclined to infer that the muscles of the abdomen and loins suffered; for it was sometimes necessary to lend assistance in order to keep patients in a sitting posture: besides they often fell heavily back on the pillows. This inference is also strengthened by the fact, that some of them constantly supported themselves with their hands, and could move forward only when in the sitting attitude.

We saw a female patient with general atrophy of the muscles, and, in addition, ptosis of the right eyelid, external strabismus, and dilatation of the pupil. Clearly, this was a case of polyneuritis with paralysis of the oculo-motor nerve. Such cases, according to Prof. Talma, occur frequently, even without any epidemic form of polyneuritis.

As to the electrical examination of the muscles, it is a matter, apparently, to which less importance is attached in England than in Holland. Dr. Rambaut, who had examined several patients electrically, informed us that, in some cases, he had not been able to obtain contractions in the muscles of the legs, either by the faradic or galvanic current. He mentioned one case where the contraction formula was modified; K. C. C. did not occur first.

To our investigation in this direction we do not attach too much importance. The time was too short, and the electrical instruments were not such as we were accustomed to use. What we did observe, however, we shall communicate. In the cases of two male and one female attendants no irregularities worth mentioning occurred. As to the other female nurse, contraction of the right m. peroneus with 4 M. A. (K. C. C.), and contraction of the left m. peroneus, with 5 M. A. (K. C. C.), no slow contractions. In the case of a girl who had been idiotic from birth, we found, with

6 M. A., insensibility to the galvanic current, not only in the muscles of the legs, but also in the muscles of the hand and the cucularis; the left sterno-cleido-mastoideus reacted at 5 M. A. (K. C. C.). The sensibility to the faradic current of all the muscles examined in the case of the latter patient was = 0.

The atrophied muscles were relaxed to the touch. In a single instance we saw that after a tap with the percussion hammer on the muscles of the calf a slow contraction followed. Of the tendon and skin reflexes only the knee reflex seemed occasionally somewhat increased; but frequently, also, in far advanced cases it had apparently disappeared altogether. Sometimes, even then, it could be obtained by the hand grip of Jendrassik; mostly it could not. After recovery it again returned (see history of Th. G.)

The joints in the parts of the body affected had become unusually relaxed, and passive mobility had been increased to an extraordinary degree. Were the patients lying on their backs, one could easily bring the heels against the gluteal regions: we even saw cases in which, when the patient was lying on his face, one could, without exertion, carry the heels against the gluteal region; the heels fell against the nates with an impact, and the legs remained in this position of extreme flexion until brought back to their normal position. When in the upright attitude, these patients could sometimes stand; but let them be put out of this attitude and they fell (weakness of quadriceps extensor). We also saw one female patient with relaxed joints to which was added *genu recurvatum*, first observed during the progress of the polyneuritis. Not only in the joints of the knee was this relaxation observed, but also in the ankle joints, and by reason of the relaxed state of the lig. arcus pedis even a form of flat foot had been developed. Relaxation of the joints, and their great passive mobility, are easily accounted for on the ground of atrophy of all the soft parts around the joints. To explain the origin of *genu recurvatum* it seems to us that one would be obliged to presuppose atrophy of the cartilages.

Speaking generally, the skin was œdematous from the very beginning. Frequently, long after the characteristic prætibial and other œdemas had vanished, the skin continued thick and stiff to the touch.

Now and then, cases presented themselves showing no œdema; but in reference to these, from the very beginning, the thought was entertained that we might have been dealing with the form of beri-beri termed by some authors the "adipose" variety.

Sometimes diffuse discolorations of the skin were observed which could not be referred to a previous lesion.

The nerves, especially the N. peroneus, were, in the few cases we examined during convalescence, not found to be thickened or painful. These phenomena are said to have been often observed in the 1894 outbreak, especially in the more serious cases. According to Dr. Rambaut, the excitability of the N. peroneus for the galvanic current had often much decreased. Not always, but particularly in 1894, inflammatory and degenerative processes in the peripheral nerves were frequently found microscopically.

The blood of the patients was frequently examined by Professor Scott and others. Professor Scott, in 1894, found, in some cases, micro-organisms apparently identical with those which at the time were pointed out by Pekelharing and Winkler as specific of beri-beri. On continued examination he failed to discover their existence.

The organs occupying the abdominal cavity, at least the spleen, liver, kidneys, presented nothing specific either during life or *post mortem*. *Post-mortem* examination revealed dilatation of the right side of the heart, degeneration of the heart muscle (the muscular tissue of this organ was flabby and degenerate—Patrick Manson), further, œdema of the lungs, often hydrops pericardii et pleuræ and anasarca; also inflammatory degeneration of some nerves and œdema of the brain were occasionally found; but, in the case of the insane, the last-named phenomenon may be regarded as of little consequence in reference to the disease in question.

It appears to us no easy task to name the disease at present engaging our attention. What remains certain is, that here we have a polyneuritis manifesting itself in an epidemic form.

We saw a few cases in which it was quite possible that the catching of a cold, or the remaining in a damp, cold apartment, might have contributed to its cause (in overcrowded wards good ventilation is impossible without the production of draughts).

A few cases might be brought under the category of inflammatory œdema (see Professor Talma's article in *Ned. Tydschrift voor Geneesk*, 1894), such as occurs not rarely, sometimes even epidemically; or under the category of a rheumatic affection (myositis, tendinitis, neuritis rheumatica); but these cases were so few as compared with those which constituted the type that they may be regarded as unimportant.

Catarrhal affections were occasionally met with, even in the initial stage.

Diphtheria occurs occasionally in Dublin; and it is well known that, though this disease may manifest rather mild, even almost unobserved angina, still paralysis may be one of its sequelæ. In these epidemics we may eliminate the possibility of such ætiological factors.

Now, as to the ætiology of the disease one fact appeared to us of the greatest importance—namely, that very many cases began with vomiting, diarrhœa, and a rise of temperature during the first few days. Hence arises the thought that a toxic agent may have originated in the gastro-intestinal canal. It is, however, certain that vomiting, diarrhœa, and fever did not, in many cases, precede the other symptoms. It appears to us possible that the epidemics of polyneuritis in the Richmond District Asylum had their origin in an intoxication proceeding from the gastro-intestinal canal. That the symptoms of vomiting and diarrhœa need not be a *conditio sine quâ non* [to such an assumption], is a matter of course.

The question now remains: What was the cause of the intoxication? What was the nature of the poison? Did it lurk in the food or in the drink? Was the poisoning due to the use of amylacea, of which so much has been written and spoken recently? Was it due to toxins of one micro-organism, or of different kinds of micro-organisms? To answer those questions it is necessary to investigate the question—By what known poisons manifestations may be caused similar to those observed in the disease which occurred in the Asylum.

Lead.—The Annual Report of the year 1895 of the Suffolk Asylum urges us seriously to examine this factor. It seemed as if the epidemic that had prevailed in the Dublin Asylum had here been repeated in a most striking manner; the difference was only a difference in degree. According to Dr. Conolly Norman, who had seen the patients in the Suffolk Asylum, the symptoms there, in 1895, were less violent than in Dublin in 1894; it was more like the Dublin epidemic of 1896-1897. Lead was found at that time in the drinking water in Suffolk, and in sufficient quantity to cause such poisoning, and found only where cases did present themselves—namely, in the female department. Dr. Norman, however, informed us that the epidemic has reappeared in Suffolk, even after satisfactory measures had been adopted to prevent lead from again being present in the drinking water.

Moreover, it appears to us strange that among so many patients not even one typical case of lead poisoning had been developed. Further, those muscles which suffer most in lead poisoning showed no special liability to become attacked; and the muscles which in lead poisoning remain free seemed to enjoy no special immunity. The well-known blue edges of the gums did not, in a single instance, appear. No lead colic. No obstinate constipation. The red edges of the gums which are described in the above-mentioned report are also observed in other acute intoxications. Last, but not least, the drinking water of the Richmond Asylum was tested several times for heavy metals, but never was any of them found in it. Also the sample of water which we brought back with us to Holland was found free from those metals.

Arsenic.—The symptoms of arsenic poisoning bear a stronger resemblance to the disease in question. It was not possible for us to decide whether this poison could have played a part here; but we can for certain state that it was not to be found in either food or drink.

Alcohol.—In consequence of our investigation as to the possibility of alcohol giving rise to the symptoms, we can safely assert that such a possibility did not exist.

Farinaceous Poisons.—The food in the Asylum may be said to have been of good quality and varied. The different varieties of food are of the same kinds as those consumed in other institutions of the city, and by the population of Dublin.

Ergotism, pellagra, acrodynia, and pelada could not, on the ground of the symptoms, be thought of. Moreover, pellagra and pelada are excluded, for maize had never been consumed in the Asylum. So also are ergotism and acrodynia; if from no other reasons, by the fact already mentioned, that the grain used in the Asylum is of the same kind consumed in other institutions and by the people of the city.

Finally, the question remains—Could this disease have been beri-beri? From the point of view that an acutely dilated right heart + anæsthesia of the legs + disappearance of the knee tendon reflex = beri-beri; or, if finding, on examination, œdemas without renal disease + brown atrophy of the heart muscle + degeneration of some nerves, one says it is beri-beri we have to deal with, then, certainly, one is almost justified in believing in the existence of beri-beri, at least as regards a great number of the cases. After an investigation of all the symptoms which occurred in the Asylum disease, and those also observed in beri-beri, possibly with many there will remain but little doubt as to the correctness of the diagnosis.

Let us be allowed to state, as our own opinion, that this disease is not beri-beri such as it manifests itself in our colonies [Dutch]. However, no affection presents more varied aspects than beri-beri (Pekelharing and Winkler); it is very difficult, nay, even impossible, to say of a given instance, "this is not beri-beri."

All that we observed may possibly be present in beri-beri occasionally; nevertheless, the opinion we have expressed as to the total impression made upon us seems to us to be not without weight. Briefly, we shall give our reasons for this opinion.

I. Never in Holland up to the present time, has a building, or even part of a building, been infected by beri-beri, notwithstanding that patients are sent in hundreds every year from the very foci of the disease; and this fact is the more important, since at no time were preventive precautionary measures adopted, nor has a case of beri-beri *de novo* hitherto been observed in Holland. The chance of the transportation of the disease to Dublin and Suffolk as compared with Holland is practically *nil.*

II. Europeans, at first, remain free from beri-beri (Colhoun and others). It is only after they have become acclimatised to the regions within the tropics, generally only after a few months, that they acquire a predisposition to the disease. Considered from this point of view, the unexpected appearance of beri-beri epidemics in Europe seems something very strange.

III. As is well known, beri-beri mostly attacks men in the full vigour of life. In Dublin, in 1894, the majority of the sufferers were men; but in 1897 more women were affected, and they were of a more advanced age. In Suffolk, in 1895, the disease was exclusively confined to women. There are very few children in the Asylum, and, consequently, they may be left out of question.

IV. The course of the first epidemic in the Richmond Asylum, beginning in the summer, and ending towards winter, agrees fairly well with the course of beri-beri in subtropical lands, such as Japan (Patrick Manson). In this respect, the two last epidemics were far less striking.. The Suffolk epidemic began about the end of December.

V. We now come to the clinical differences. Vomiting and diarrhœa with fever, as initial symptoms, are observed occasionally in beri-beri; but, comparatively speaking, they appeared far more prominently in the disease in Dublin and Suffolk.

VI. The anæsthesiæ were entirely different from those we observed in cases of beri-beri in our colonies. The anæsthetic spots on the legs and elsewhere, which constantly changed their positions, and altered in intensity, often disappearing even within an hour—these with the hyperæsthetic zones do not at all agree with the symptom, so prominent in the East Indies, of anæsthesia or hyperæsthesia over the whole leg. The latter slowly appear and slowly disappear. A hair can be plucked [from the leg] without producing pain, as everyone knows who has lived in or around Atjeh.

VII. In the disease under review the œdema was, indeed most prominent on the legs; but then, sparing the dorsa of the feet, it frequently formed a manchette. In the beginning, too, it was accompanied by slight œdema over the sacrum and sternum, with a great tendency to anasarca. Here, in point of localisation, there is a difference; for, in the great majority of the beri-beri patients, the prætibial œdema extended to the dorsum of the foot, and anasarca was not well marked. Moreover, the fact that the œdemas frequently disappeared rapidly, the atrophy of the muscles thereby becoming suddenly apparent, is not in accord with what has been observed in beri-beri.

VIII. The action of the heart was such as one would expect in beri-beri. One symptom, however, we never observed, notwithstanding that we examined a great number of patients in order to find it—the diffuse heart pulsation. In beri-beri, in the acute stage if one lays the hand flat over the cardiac region, one ascertains that in 50 per cent. of cases, possibly in more, the area of the normally sharply circumscribed impulse cannot be defined, though a strong diffused pulsation is felt. Some medical men, when through circumstances forced to decide in haste, diagnosticate beri-beri through the clothes, so pronounced is this sign.

IX. The atrophy of the muscles was not such as is found in beri-beri. The muscles of the arms were oftener affected. So many cases of dropped wrist are not generally met with in beri-beri (in Suffolk Asylum this symptom occurred even more frequently than in the Dublin epidemics). Also, the number of patients with atrophied muscles of the legs, relatively speaking, seemed to us uncommonly large. It was with alarm we contemplated the possibility of so large a percentage of unfortunate people afflicted with dropped feet, contractures, and complete paralysis among those who are the victims of beri-beri in our colonies. A wretched state of affairs it would be for the hundreds and thousands who are there attacked by the disease. To carry out the comparison fairly, we would have to add to the typical cases of beri-beri innumerable cases of tachycardia and other abortive forms. The atrophies of the muscles were often much more marked than the state of the organs of the chest would lead one to infer. We saw an insane patient with total paralysis of the legs, moving on his knees at full speed through the corridor, and crying loudly without becoming breathless. His heart and lungs were normal.

X. In beri-beri we never met with, to such a degree, the extreme relaxation of the joints as it occurred in the Dublin epidemic. Only very extensive atrophy of all the soft parts around the joints can explain this phenomenon. In fact this symptom appeared to us to plead rather *against* than *for* beri-beri..

However, Patrick Manson, in his monograph on beri-beri, lays emphasis on the relaxed state of the joints. He also describes anæsthetic patches of the skin of the legs, and similar spots over the body. He does not make any definite statement as to their duration and variability. He mentions paræsthesia similar to that observed in Dublin, great hyperæsthesia over the tibial region, even on a slight touch, and a frequent occurrence of paralysis and contractures as a persistent residuum.

We do not consider it improbable that beri-beri may present a type different from that of our colonies. Such is known of other diseases due to degeneration of the nerves. For instance, the gangrenous form of ergotism manifested itself mainly in western Europe, whereas the spasmodic form occurred most frequently in eastern regions; yet, both forms sprang from a common cause.

We repeat what has been already said, that the Dublin disease should be considered as a variety of polyneuritis. But, between this particular form of polyneuritis and that called beri-beri in our colonies, there exist marked differences.

Owing to the brief time that was at our disposal for investigation, we have not been able to decide as to what was the cause of the epidemic in the Dublin Asylum: nor have the physicians there been able, up to the present, to determine it. This is not a matter to be surprised at. The causes of polyneuritis are manifold; to decide for every epidemic which of the known causes has originated it, is, indeed, a very difficult task. Nor should it be forgotten that one may conceive causes of polyneuritis, hitherto unrecognised.

Though different in the complexes of their symptoms, in order to be able to decide whether the two diseases—that in our colonies and that seen in the Dublin epidemic—are, in reality, of a like nature, it would be necessary to know how both are caused. "True knowledge is the knowledge of causes" (*Het ware kennen is het kennen der oorzaken*).

What was the cause we did not ascertain in Dublin; but that alone could justify a final decision. From our observation all we can say is, that the beri-beri which occurs in our colonies creates a totally different impression from that brought home by us from Dublin.

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